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From the London Hospital Medical College and St. Bartholomew's Hospital

THE PSEUDOCHOLINESTERASE VARIANTS. ESTERASE LEVELS AND DIBUCAINE NUMBERS IN FAMILIES SELECTED THROUGH SUXAMETHONIUM SENSITIVE INDIVIDUALS

By H. HARRIS, M. WHITTAKER, H. LEHMANN and E. SILK

The discovery of inherited differences in the formation of pseudocholinesterase arose from the study of individuals who were found to be unusually sensitive to the muscle relaxant suxamethonium. This drug is frequently administered during surgery or electro-convulsive therapy and in most people has only a short duration of action. Occasional individuals however when given the drug in its usual dose show a much more prolonged response. Such people were found to have lower levels of pseudocholinesterase activity than were found in most other people (*Bourne, Collier and Somers* 1952; *Evans, Gray, Lehmann and Silk* 1952, 1953), and *Lehmann and Ryan* (1956) observed that low pseudocholinesterase levels might also be found among some of their immediate relatives who were otherwise healthy. Family studies (*Lehmann and Ryan* 1956; *Lehmann and Simmons* 1958; *Kaufman, Lehmann and Silk* 1960), led to the hypothesis that suxamethonium sensitive individuals with low pseudocholinesterase activity were homozygous for an uncommon gene, which in heterozygotes also resulted in a depression of pseudocholinesterase levels but to a lesser degree. The three genotypes postulated on this hypothesis could not be sharply differentiated in terms of pseudocholinesterase levels presumably because of the variation within each genotype, and overlapping of the three distributions. The assay of pseudocholinesterase in these studies was carried out mano-

metrically using acetylcholine as the substrate. It was concluded that individuals with values of greater than 90 units (one unit equals one μl CO_2 liberated by 1 ml serum in one minute at 37° C) were normal homozygotes, individuals with values below 20 units were abnormal homozygotes, and individuals with values between 36 and 60 units were heterozygotes. However, in the range 60–90 units both normal homozygotes and heterozygotes might occur and similarly in the range 20–36 units both heterozygotes and abnormal homozygotes might be found.

Meanwhile *Kalow and his colleagues* (*Kalow and Genest* 1957; *Kalow and Staron* 1957; *Kalow and Gunn* 1959; *Kalow and Davis* 1958; *Kalow* 1959), had developed a different approach to the problem. They compared the behaviour of the cholinesterase present in the sera of a number of individuals who were suxamethonium sensitive, and that in a number of normal subjects, towards a variety of substrates and inhibitors. It emerged that in certain respects the pattern of reactions differed markedly in the two groups of individuals, and it was concluded that the cholinesterase enzyme protein present in the sera of the suxamethonium sensitive individuals was in some way qualitatively different from that present in most other people. A simple technique for differentiating between the two sorts of enzyme was devised which involved the measurement of the degree of inhibition produced by a given concentration of the cholinesterase inhibitor dibucaine (percaine) under certain standard conditions. The substrate in this procedure is benzoylcholine and the reaction is followed spectrophotometrically. The percentage inhibition of the rate of hydrolysis of benzoylcholine under the standard conditions was called the dibucaine number, and this was found to be very much less in sera from suxamethonium sensitive individuals than in sera from most other people. The dibucaine number for any one individual appears to be relatively constant and is independent of variations in the level of his pseudocholinesterase activity.

An extensive survey of randomly chosen individuals revealed that the distribution of dibucaine numbers in the general population was trimodal. Most individuals gave values clustering round a mode of DN = 79. A second group (about 3 percent of the population) clustered round a mode of DN = 62 and there was a third group of relatively rare individuals with values of the order of DN = 16. It was to this third group that the individuals discovered because of their unusual sensitivity to suxamethonium were found to belong. The three phenotypes defined by this trimodal distribution were referred to as "usual", "intermediate" and "atypical" respectively. It was suggested that the three phenotypes were determined by a pair of allelic genes, individuals with the "usual" phenotype being

homozygous for one of them, individuals with the "atypical" phenotype being homozygous for the other, and individuals with the "intermediate" phenotype being heterozygous. The common allele could be regarded as determining the "usual" enzyme, and the relatively rare allele as determining the "atypical" enzyme. The findings in the heterozygotes were consistent with a situation in which both enzymes were formed in approximately equal amounts.

In examining the behaviour of the two enzymes with a series of different cholinesters (*Kalow* 1959) it was found that the Michaelis constants of these esters and the atypical enzyme were different from the respective constants observed with the usual enzyme, though the degree of difference varied from substrate to substrate. The findings implied a decreased apparent affinity of the atypical esterase for each of these substrates and one would expect therefore to find in sera containing only the atypical enzyme a lower level of esterase activity as measured by the rate of hydrolysis of any one of these substrates (for example acetylcholine) than in a serum containing only the "usual" enzyme, even if the concentration of enzyme molecules present in the two sera were the same. Thus the "familial pseudocholinesterase deficiency" observed by *Lehmann and his colleagues* in succinylcholine sensitive individuals and their relatives could on this hypothesis be interpreted as due to the replacement of the usual by the "atypical" enzyme.

In view of this it seemed desirable in attempting to study these inherited variations in pseudocholinesterase formation further, to examine a series of families using both approaches to the problem. This was the purpose of the present investigation. The families were each selected by the occurrence of an individual known to be unusually sensitive to suxamethonium. The serum cholinesterase in each individual was examined both in terms of dibucaine inhibition, and in terms of enzyme activity as measured by acetylcholine hydrolysis.

Another point of interest which requires further clarification concerns the genetics of the variations as defined by dibucaine number. *Kalow and Staron's* (1957) conclusion about the genetics of the three dibucaine number phenotypes was largely based on two extensive pedigrees in which all three phenotypes were segregating. There was however in these families one exception to the expected familial distribution. The mother of one of the individuals with the atypical phenotype, was found to have the "usual" phenotype, the father being "intermediate". This anomalous finding suggested that the genetical situation could on occasion be more complex and that possibly other alleles or modifying genes might play a significant

part in determining the phenotype. The examination of a series of families selected by propositi with the "atypical" phenotype might be expected to indicate how frequently such anomalous segregation patterns occur, and perhaps throw further light on the nature of the modifying factors involved.

Material and methods

Sera from 69 individuals in 11 unrelated families were studied. Each family was selected by the occurrence of one individual who had been found to have an excessively long prolonged apnoea when suxamethonium was administered during surgery.

Dibucaine numbers were determined manometrically (*McArdle* 1940). Cholinesterase activity using acetylcholine as substrate was determined spectrophotometrically by the method of *Kalow and Davies* (1957).

Results

Fig. 1 shows the distribution of dibucaine numbers among the 69 individuals in the 11 families studied. The distribution is clearly trimodal and the three phenotypes defined by *Kalow and his colleagues* can be readily identified. The mean DNs for each phenotype (Table 1) correspond quite closely to the values of 79, 62 and 16 reported by *Kalow and Staron* (1957). All the 11 propositi selected because of suxamethonium sensitivity were found to belong to the "atypical" phenotype.

Fig. 2 shows the distribution of pseudocholinesterase levels estimated manometrically using acetylcholine as substrate. The distribution is continuous with no clear cut separation into distinct phenotypes, though all

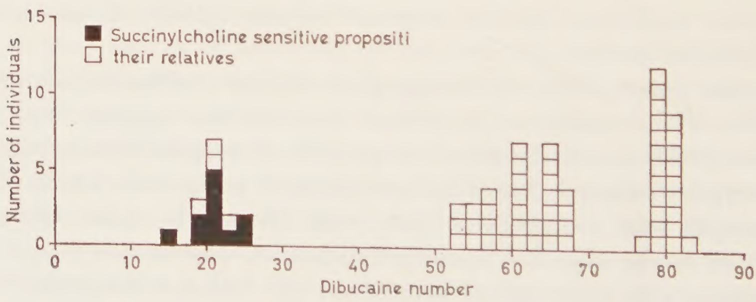


Figure 1

Distribution of dibucaine numbers. Suxamethonium sensitive propositi, black, their relatives white squares.

Table 1. Means, standard deviations and ranges of the dibucaine numbers for the three phenotypes

Phenotype	Number of Individuals	Mean Dibucaine Number	S. D.	Range
Usual	23	79.30	1.16	76–82
Intermediate	31	60.42	4.66	52–67
Atypical	15	20.33	2.66	14–25

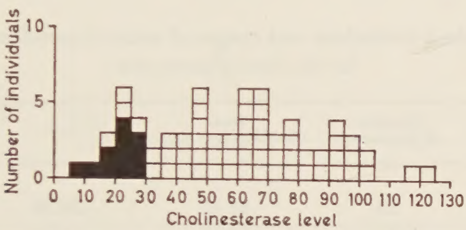


Figure 2

Distribution of pseudocholinesterase levels (acetylcholine substrate).

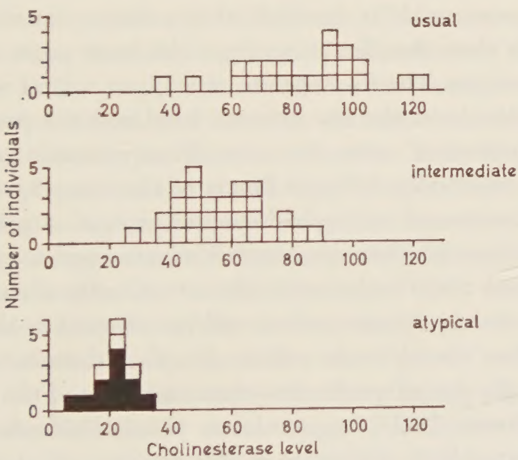


Figure 3

Distribution of pseudocholinesterase levels in the three phenotypes defined by the dibucaine numbers.

the propositi have values at the lower extreme of the distribution. However, if the data are subdivided into the three phenotypes defined by the dibucaine numbers then it can be seen (Fig. 3) that the continuous distribution can be regarded as being made up of three separate but overlapping distributions. The means and standard deviations for these three distributions are given in Table 2. The "atypical" phenotype defined by determination of dibucaine numbers has on the average a much lower level of esterase activity as measured with acetylcholine as substrate, than does the "usual" phenotype. The "intermediate" phenotype is also intermediate in terms of esterase activity.

Table 2. Means, standard deviations and ranges of units of pseudocholinesterase activity in the three phenotypes

Phenotype	Number of Individuals	Mean Cholinesterase activity	S. D.	Range
Usual	23	83.48	20.20	38–124
Intermediate	31	56.06	14.30	26– 86
Atypical	15	21.47	6.55	7– 33

The overall correlation between the two sets of measurements is shown in Fig. 4. It seems reasonable to conclude that a large part of the variance in esterase levels in these families arises from the same cause as the variation in dibucaine numbers. The findings are clearly consistent with the suggestion of *Kalow* that both the low esterase level and the peculiar inhibition characteristics observed with the sera from suxamethonium sensitive individuals are essentially different facets of the same basic phenomenon, namely the occurrence of an atypical enzyme protein. A greater variability of esterase level than of dibucaine number within any one phenotype is not surprising, because while variations in the overall rate of enzyme synthesis, which might be due to diverse causes, will be reflected in the estimation of esterase level, they would not be reflected in the dibucaine numbers which measure essentially one of qualitative characteristics of the enzyme.

Kalow and Staron (1957) suggest that the individuals of the "intermediate" phenotype have a mixture of both the "usual" and the "atypical" enzymes in their sera. The significantly greater variation in dibucaine numbers among individuals of this phenotype as compared with the other two phenotypes is attributed to variation in the relative proportion of the

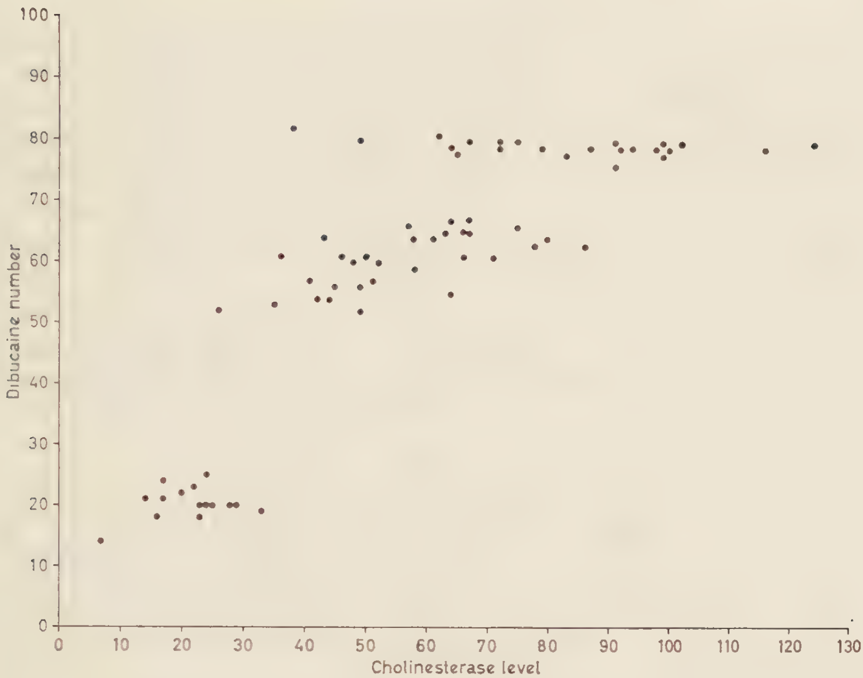


Figure 4

Correlation of dibucaine numbers with pseudocholinesterase levels.

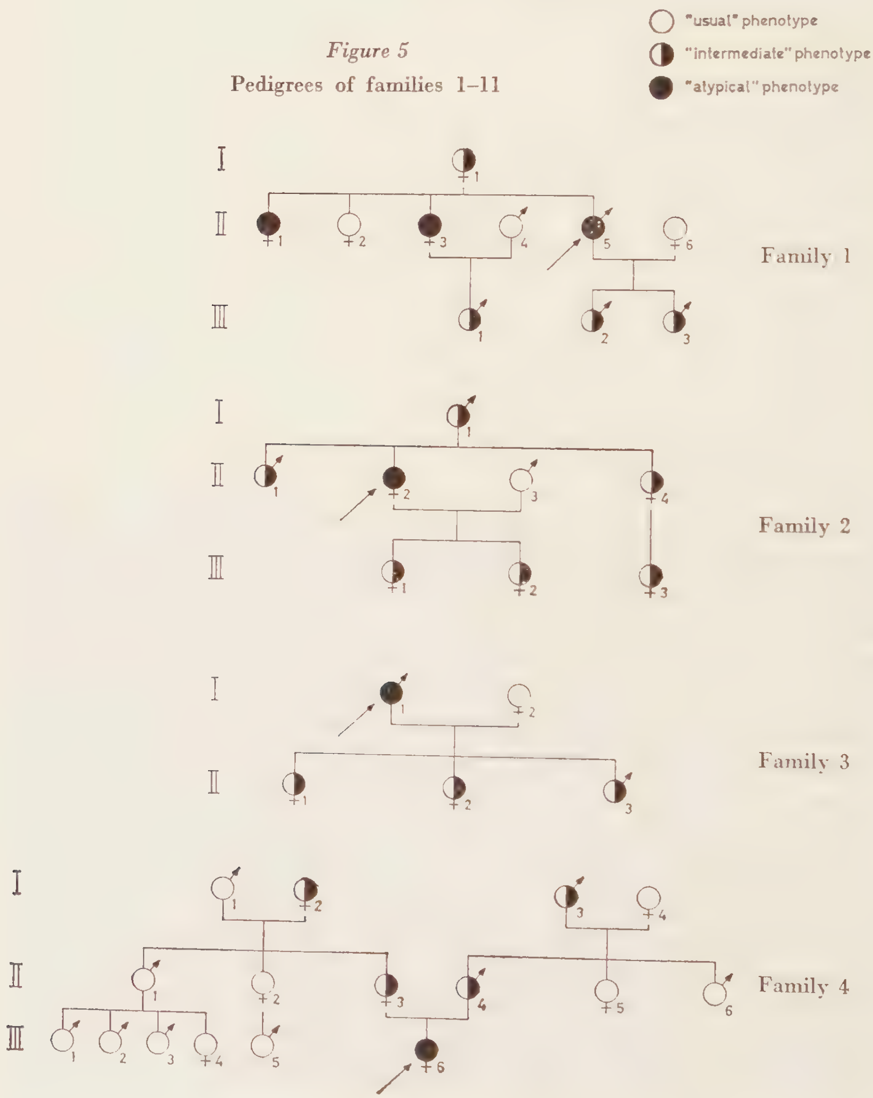
two enzymes present in different individuals. This point can be examined in the present data in the following way. If individuals of the intermediate phenotype differ in the proportion of the two enzymes present, then there should be a positive correlation between dibucaine numbers and esterase levels within this phenotype. This is so because individuals in whom the "usual" enzyme preponderated would tend to have high dibucaine numbers and also relative high esterase levels, while those in whom the "atypical" enzyme preponderated would tend to have low dibucaine numbers and relatively low esterase levels. On the other hand there would be no reason on this hypothesis to expect any marked correlation between the dibucaine numbers and the esterase levels within the "usual" or the "atypical" phenotypes. In the present data there is in fact a highly significant positive correlation between dibucaine numbers and cholinesterase level in the "intermediate" phenotype ($r = 0.65$, $p = <.001$). Neither of the equivalent correlation coefficients for the other two phenotypes are significant.

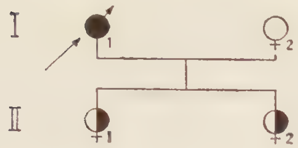
The familial distribution of the three phenotypes in the series of families studied here is given in Fig. 5. The individual dibucaine numbers and

cholinesterase levels are given in the appendix. The hypothesis that individuals of the "atypical" phenotype are homozygous for a relatively rare gene, for which individuals of the "intermediate" phenotype are heterozygous, requires that none of the parents or children of "atypical" individuals should have the "usual" phenotype. The relevant data are shown in Table 3. There is one exception to the expected pattern. This occurs in family 6. I_2, the mother of two "atypicals" (II_2 and II_3) has the "usual"

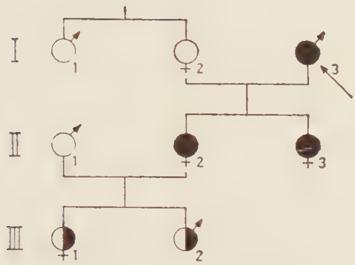
Figure 5

Pedigrees of families 1–11

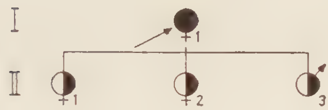




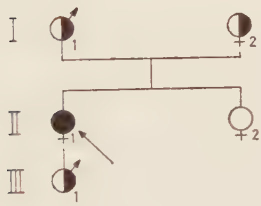
Family 5



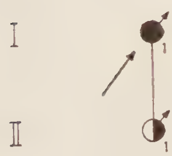
Family 6



Family 7

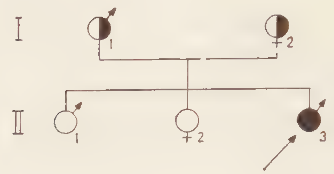


Family 8

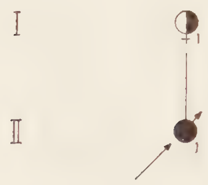


Family 9

phenotype. Her husband I_3 has the "atypical" phenotype. Since in this family it is the mother who has the exceptional phenotype one can exclude illegitimacy as a cause of the unexpected segregation pattern and one must conclude that the genetical situation here is inconsistent with the hypothesis in its simple form. However, the segregation data in all the other families are completely consistent with the hypothesis.



Family 10



Family 11

Table 3. Phenotypes of the parents and of the children of individuals with the "atypical" phenotype

	Phenotype			
	Usual	Intermediate	Atypical	Total
Parents	1	9	1	11
Children	–	17	2	19

The exception noted in family 6 is similar to that observed by *Kalow and Staron* in one of the matings in their family Y. Here an "atypical" individual was derived from a mating between an a father with the intermediate phenotype and a mother of the "usual" phenotype. It is apparent that although most of the family data about these phenotypes can be explained in terms of a simple two allele hypothesis, exceptions to this do occur with an appreciable frequency. Perhaps the simplest explanation of the anomalous findings is that they are due to the occurrance of a rare allele with unusual properties. For example *Kalow and Staron* (1957) have suggested that a series of alleles determining the formation of "usual" type esterase at different rates, may occur. The extreme of such a series would be an allele which led to such a low rate of esterase formation that it could be regarded as virtually inactive. Such an allele in heterozygous combination with the "usual" type allele would be expected to result in a serum giving a "usual" phenotype dibucaine number but a low total esterase activity. In heterozygous combination with an "atypical" allele one would expect an "atypical" phenotype with a low esterase activity. In family 6, for example, the

anomalous I_2 might have such an allele in combination with the "usual" type allele, and her two children II_2, and II_3 might have this allele in combination with an "atypical" allele, which they had obtained from the father I_3. The esterase level of I_2 was 65 units which is about 1 standard deviation below the mean esterase level (83 units) for the "usual" phenotype. The esterase levels of II_3 and II_2 were 16 and 7 which are respectively about 1 and 2 standard deviations below the mean for the atypical phenotype (21.5 units). The values for the esterase levels are therefore in the direction required by this kind of hypothesis.

However, other hypotheses postulating, for example, variants of the "atypical" allele with special properties, or modified genes at other loci can also be constructed to account for the anomalous findings. Unfortunately it is not possible with the data at present available to devise critical tests to distinguish between them. The study of further families showing such exceptional segregation patterns is obviously necessary. It may also be anticipated that investigation of the enzyme present in the anomalous individuals using a wider range of substrates and inhibitors would be of help in elucidating the problem.

Summary and Conclusions

(1) Cholinesterase activities measured with acetylcholine as substrate, and dibucaine numbers (% inhibition of benzoylcholine hydrolysis by dibucaine) have been determined for the pseudocholinesterase in 11 unrelated individuals who were suxamethonium sensitive, and in 58 of their immediate relatives.

(2) The distribution of dibucaine numbers was trimodal and the individuals could be unequivocally classified into the three phenotypes "usual", "intermediate" and "atypical". All the suxamethonium sensitive individuals belonged to the "atypical" phenotype.

(3) The distribution of cholinesterase activities was continuous with the suxamethonium sensitive individuals at the lower extreme of the distribution. The distribution could be subdivided into three overlapping distributions by classifying the individuals into the three phenotypes defined by the dibucaine numbers. The mean esterase levels, for the three phenotypes were: "usual" 83 units, "intermediate" 56 units, and "atypical" 21 units.

(4) There was a highly significant positive correlation between the dibucaine numbers and the cholinesterase levels within the "intermediate" phenotype. There was no significant correlation within the other phenotypes.

(5) The results are consistent with the hypothesis that the "atypical" and the "usual" phenotypes possess qualitatively distinct forms of cholinesterase, and that the intermediate phenotype has a mixture of these.

(6) With one exception, the familial distributions were consistent with the hypothesis that the three phenotypes are determined by a pair of allelic genes, the intermediate phenotype representing the heterozygote. In the exceptional family two "atypical" individuals were the progeny of a mother with the "usual" phenotype and a father with the "atypical" phenotype. This suggests that further alleles, or "modifying" genes at other loci may play a part in determining the character of the pseudocholinesterase.

Zusammenfassung

Im Serum von 11 nicht miteinander verwandten, Succinylcholin-sensitiven Personen sowie 58 ihrer direkten Verwandten wurden die mit Acetylcholinsubstrat gemessene Cholinesteraseaktivität und die dibucainen Zahlen bestimmt (prozentuale Hemmung der Benzoylcholinhydrolyse durch Dibucain).

Die Verteilung der dibucainen Zahlen war trimodal, und die Personen konnten eindeutig in drei Phänotypen eingeteilt werden: «normale», «intermediäre» und «atypische». Alle Succinylcholin-sensitiven Personen gehörten dem «atypischen» Phänotyp an.

Die Verteilung der Cholinesteraseaktivität verlief bei den Succinylcholin-sensitiven Personen kontinuierlich am unteren Extrem der Verteilung. Die Verteilung konnte in drei sich überschneidende Gruppen unterteilt werden, indem man die Personen in die drei durch die dibucainen Zahlen bestimmten Phänotypen einordnete. Der durchschnittliche Esterasespiegel für die drei Phänotypen betrug 83 Einheiten für die «normalen», 56 Einheiten für die «intermediären» und 21 Einheiten für die «atypischen».

Der intermediäre Phänotyp wies eine äußerst signifikante positive Korrelation zwischen den dibucainen Zahlen und dem Cholinesterasespiegel auf, während bei den anderen Phänotypen keine signifikante Korrelation festgestellt werden konnte.

Diese Ergebnisse lassen sich mit der Hypothese vereinbaren, daß die «atypischen» und «normalen» Phänotypen qualitativ bestimmte Formen von Cholinesterase besitzen, der «intermediäre» dagegen eine Mischung darstellt.

Die familiäre Verteilung entsprach mit nur einer Ausnahme der Hypothese, daß die drei Phänotypen von einem Paar alleler Gene bestimmt wer-

den, wobei der intermediäre Phänotyp den Heterozygoten darstellt. Bei jener einen Familie jedoch hatten eine Mutter mit «gewöhnlichem» und ein Vater mit «atypischem» Phänotyp zwei Kinder mit ebenfalls «atypischem» Phänotyp. Man vermutet deshalb, daß weitere Allele oder «modifizierende» Gene an anderen loci für den Typ der Serumcholinesterase verantwortlich sind.

Résumé

(1) Chez 11 malades sensibles à la succinylcholine et chez 58 de leurs proches parents on a examiné la cholinestérase du sérum en se basant sur l'activité cholinestérasique mesurée par l'acétylcholine comme test et par le dibucaïne-chiffre (percaïne) (pourcentage d'inhibition de l'hydrolyse de la benzoïlcholine par le dibucaïne.)

(2) La distribution du dibucaïne-chiffre était trimodale et permettait de classer les individus d'une façon certaine en trois phénotypes «habituel», «intermédiaire» et «atypique». Tous les individus sensibles à la succinylcholine appartiennent au phénotype «atypique».

(3) La distribution de l'activité cholinestérasique correspondait aux individus sensibles à la succinylcholine à l'extrême inférieure de la distribution. La distribution a pu être subdivisée en 3 distributions se chevauchant, en classant les individus en trois phénotypes définis par le dibucaïne-chiffre. Le taux moyen de l'estérase pour les trois phénotypes était: «habituel» 83 unités, «intermédiaire» 56 unités et «atypique» 21 unités.

(4) Il existe une corrélation positive hautement significative entre le dibucaïne-chiffre et le taux de cholinestérase pour le phénotype «intermédiaire». Par contre, il n'y a pas de corrélation significative avec les autres phénotypes.

(5) Les résultats corroborent l'hypothèse que les phénotypes «atypique» et «habituel» possèdent des formes de cholinestérase nettement différentes et que le phénotype «intermédiaire» en est un mélange.

(6) La distribution familiale, à l'exception d'un cas, confirme l'hypothèse que les trois phénotypes dépendent d'une paire de gènes allèles et que le phénotype «intermédiaire» représente l'hétérozygote. Dans la famille qui fait exception à cette règle, deux individus «atypique» ont une mère du phénotype «habituel» et un père du phénotype «atypique». Ceci fait penser que d'autres allèles ou gènes modificateurs localisés ailleurs puissent jouer un rôle dans la détermination du caractère cholinestérasique.

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APPENDIX

Family	Individual	Cholinesterase Units	Dibucaine number	Comments
1	I_1	66	61	
	II_1	24	20	
	II_2	101	79	
	II_3	22	23	
	II_4	72	79	
	II_5	25	20	Propositus
	II_6	62	81	
	III_1	42	54	
	III_2	51	57	
	III_3	64	55	
2	I_1	63	65	
	II_1	78	63	
	II_2	23	20	Propositus
	II_3	116	79	
	II_4	57	66	
	III_1	58	59	
	III_2	71	61	
	III_3	86	63	
3	I_1	14	21	Propositus
	I_2	91	76	
	II_1	64	67	
	II_2	26	52	
	II_3	35	53	
4	I_1	102	80	
	I_2	44	54	
	I_3	50	61	
	I_4	99	78	
	II_1	75	80	
	II_2	83	78	
	II_3	67	65	
	II_4	67	67	
	II_5	72	80	
	II_6	79	79	
	III_1	99	80	
	III_2	87	79	
	III_3	94	79	
	III_4	98	79	
	III_5	91	80	
	III_6	24	25	Propositus

Family	Individual	Cholinesterase Units	Dibucaine number	Comments
5	I_1	33	19	Propositus
	I_2	124	80	
	II_1	61	64	
	II_2	80	64	
6	I_1	64	79	
	I_2	65	78	
	I_3	28	20	Propositus
	II_1	92	79	
	II_2	7	14	
	II_3	16	18	
	III_1	41	57	
	III_2	49	52	
7	I_1	20	22	Propositus
	II_1	58	64	
	II_2	45	56	
	II_3	49	56	
8	I_1	43	64	
	I_2	75	66	
	II_1	17	24	Propositus
	II_2	67	80	
	III_1	46	61	
9	I_1	23	18	Propositus
	II_1	66	65	
10	I_1	36	61	
	I_2	48	61	
	II_1	49	80	
	II_2	38	82	
	II_3	17	21	Propositus
11	I_1	52	60	
	II_1	29	20	Propositus

Allison, A. C. and Barnicot, N. A.: Acta genet. *10* : 17—23 (1960)

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HAPTOGLOBINS AND TRANSFERRINS IN SOME EAST AFRICAN PEOPLES

By A. C. ALLISON and N. A. BARNICOT

Genetically controlled variations of the haptoglobins, a fraction of the α_2 serum globulins, were described by *Smithies* (1955) and *Smithies and Walker* (1956), and later workers showed that the inheritance of the three commonest phenotypes depends on two allelic genes, Hp^1 and Hp^2. *Allison* (1959) has reviewed the literature. A variant of type 2–1, known as 2–1 (mod), was reported by *Connell and Smithies* (1959) but the genetics of this type is not yet clear. *Allison, Blumberg and ap Rees* (1958) found that in about 30% of subjects from Southern Nigeria haptoglobins were not detectable by benzidine staining of the starch gel, and occasional cases have been reported in European subjects. *Barnicot, Garlick,* and *Roberts* (1960) found comparably high frequencies of this phenotype in Northern Nigerians, but *Barnicot* et al. (1959) found less than 5% in some South African peoples. In family material from the former they could find no evidence that this haptoglobin-negative type was inherited and suspected that, at least in populations in which it is very common, environmental factors play a major part.

Smithies (1959) described a β-globulin variant which moved more slowly than the usual type in starch gel electrophoresis; he found a number of examples in both American Negro and Australian aboriginal material, and he and *Hiller* (1959) presented evidence that this variant, TfD_1, is simply inherited. Other variants of these iron-binding β-globulins, or transferrins, have been described and the subject is reviewed by *Giblett* et al. (1959).

Substantial differences in the haptoglobin gene frequencies of different populations have been shown to exist (*Allison, Blumberg and ap Rees,*

1958, *Barnicot* et al. 1959, 1960, *Giblett* 1959, *Harris, Robson, Siniscalco*, 1959, *Sutton* et al., 1959), but relatively few have been examined, and in the case of Africa more data are needed before a clear picture of the distribution can be achieved. The present paper deals with some tribes from East Africa, a region which has not previously received attention.

Material and Methods

The bulk of the material was collected from Baganda subjects. Sample 1 was obtained from hospital out-patients suffering from minor illnesses and injuries. Sample 2 was obtained from Red Cross blood donors. There is also a small sample of miscellaneous Bantu tribes of Uganda from the same source, and this is listed separately. In addition there is a sample of 50 adult Masai and 60 Bondei, 51 of the latter being children aged 4 months to 4 years.

The Baganda are the largest tribal unit in Uganda: they are a Bantu-speaking agricultural people living in an area at the north-western edge of Lake Victoria. Although the Baganda may have received some infiltration of caucasoid people from the north-east no clear division of the population into a physically distinct ruling group of Hima and a more negroid servile class, as in the neighbouring territories of Ankole and Ruanda, is found. The Masai are a Nilo-Hamitic speaking pastoral tribe who nomadise over an extensive zone stretching from Kenya into Tanganyika. They differ from adjacent negro peoples in their tall stature, somewhat caucasoid facial features and relatively light skin colour. The Bondei are a small group of Bantu belonging to the Zaramo group, who occupy the foothill region opposite the island of Pemba on the Tanganyika coast. Although considerable mixture with Arabs has occurred in the case of the nearby coastal Swahili this influence is less apparent in the Bondei.

The sera were brought or sent to London by air and were stored at -20°C. After adding haemoglobin to saturate the haptoglobins a small amount was soaked up on a small piece of 3MM Whatman paper and a dozen of these were inserted four in a line into a wide gel. The gel was prepared from B.D.H. potato starch hydrolysed by the method of *Smithies* (1955). The discontinuous tris-borate buffer system described by *Poulik* (1957) was used since this procedure permits all haptoglobin types and also transferrin variants to be scored without confusion. Examples of TfD_1 were compared in parallel against a specimen of this variant kindly identified by Dr. *O. Smithies*, and the Nitroso-R reagent of Smithies was used to check the identity of the variants as iron-binding proteins. One

half of the starch gel was routinely developed with the benzidine-hydrogen peroxide reagent and the other was stained directly with amidoschwarz B.

Results

The haptoglobin and transferrin phenotypes are summarised in the table below:

Table 1

Haptoglobins and Transferrins of East Africans

Tribe		Total	Haptoglobin phenotypes					Haptoglobin gene frequencies %		Transferrin phenotypes		
			1–1	2–1	2–1 (mod)	2–2	Neg.	Hp^1	Hp^2	CC	CD_1	D_1
Baganda	Sample 1	90	26	20	9	10	25	62.3	37.7	87	3	0
	Sample 2	75	21	34	1	4	15	64.2	35.8	73	2	0
	Total	165	47	64		14	40	63.2	36.8	160	5	0
Miscellaneous Bantu*		26	4	12	4	2	4			26	0	0
Bondei	Children	51	8	18	3	11	11	46.2	53.8	47	4	0
	Adults	9	2	3	0	3	1			8	1	0
Masei		50	10	22	1	12	5	47.8	52.2	50	0	0

*Basoga 16, Nyankole 4, Gwere 2, Banyoro, Batoro, Bakiga, Bagishu one each.

The two Baganda samples are shown separately because they are not homogeneous ($\chi^2 = 14.4$, d.f.4, $P = 0.01$). The difference is mainly due to the high frequency of type 2–1 (mod) in Sample 1 and the excess of type 2–1 in Sample 2. For the calculation of haptoglobin gene frequencies types 2–1 and 2–1 (mod) are however combined, because the genetics of the latter are uncertain and the combined values usually satisfy equilibrium conditions. The heterogeneity between Samples 1 and 2 disappears when this is done and, with due reservation, we have given phenotype frequencies and gene frequencies for the total Baganda sample obtained by pooling them. The frequency of Hp^1 in the Baganda is around 0.60, a figure which is in the range of values reported for West Africans and rather higher than the frequencies reported by *Barnicot, Garlick, Singer and Weiner* (1959) for Bushmen and Zulus. The frequency of haptoglobin-negatives is only a little lower than that found in West Africans.

The haptoglobin gene frequencies of the Masai and Bondei are very similar and even on these small samples they are significantly different

from those of the Baganda, the Hp^1 frequency being a little below 0.50. In the Masai there were only 10% of haptoglobin-negatives while in the Bondei the figure (24.2%) approaches that found in the Baganda.

The frequency of the heterozygous transferrin type CD_1 is lower in the Baganda than in Nigerians or in Bushmen and at approximately the same level as in the Zulu of South Africa. This variant was not found in the Masai sample.

Two anomalous cases which have not been included in the table must be mentioned. In one of these (Baganda Sample 2) there was a single strong haptoglobin band similar to that in type 1–1 but it was at a level between the first and second $\alpha\beta$ bands. The specimen also showed a single transferrin band which was at a level considerably behind the usual position of TfD_1. In the other specimen (Baganda Sample 1) there was also a single transferrin band which was somewhat slower than TfD_1 but a little faster than that in the specimen described above; four benzidine positive bands occurred in the $\alpha\beta$ region, the first being the strongest as in type 2–1, but each of them was noticeably slower than the bands in this type. Until repeat specimens can be obtained and also family material, it must remain uncertain whether these two cases, showing abnormalities in both haptoglobin and transferrin migration rates, are artifactual or whether they are new inherited variants.

Some of the Baganda subjects (Sample 1) and Bondei children were also tested for glucose-6-phosphate dehydrogenase (G6PD) activity in the erythrocytes (*Allison* 1960). The sex-linked trait in which G6PD activity is markedly reduced was found to be common in East African tribes from malarious regions; thus the gene frequency was 27.3% in the Bondei and 15.0% in the Ganda but only 1.7% in the Masai. Since this trait predisposes carriers to haemolysis on exposure to various drugs and to fava beans (*Beutler* 1959), it is possible that they would be subject to haemolysis initiated by some factor in the African diet or environment, and this might lead to depletion of haptoglobins. *Siniscalo* (1959) has suggested that this may be so in parts of Sardinia where G6PD deficiency is common. The results of G6PD tests on Baganda adults and Bondei children are shown in relation to haptoglobin types in Table 2.

In the Bondei sample there were 31 males with 22.6% G6PD deficiency and 20 females with 10% G6PD deficiency: the corresponding figures for the Baganda adults were 66 males (15.1% G6PD deficient) and 19 females (5.3% G6PD deficient). In both samples cases of enzyme deficiency are more frequent among haptoglobin-negatives than in other haptoglobin types. Even if the samples are pooled, however, the proportion among

Table 2

Numbers of normal (+) and G6PD deficient (–) subjects in East Africans in relation to haptoglobin type

Sample	No.	1–1		2–1		2–2		Negative	
		+	–	+	–	+	–	+	–
1. Bondei	51	6	1	19	3	10	1	7	4
2. Baganda	85	22	2	24	4	10	1	18	4
1 and 2	136	28	3	43	7	20	2	25	8

haptoglobin-positives (11.6%) is not significantly different from that in haptoglobin-negatives (24.2%) at the 0.05% level. Although there is a suggestion of some relationship, more data, which would also permit detailed analysis in terms of age and sex, is needed to establish it. It seems clear in any case that G6PD deficiency cannot be the only factor responsible for haptoglobin depletion in Africans though it may be a contributory factor.

Discussion

The data on the anthropometry of the Baganda and other East African tribes have been summarised by *Oschinsky* (1954) but information on simple genetical traits in the Masai and Baganda is restricted to the AB0 groups and a full discussion of their biological characteristics in the light of historical facts and theories is scarcely warranted at this stage. It is perhaps surprising that the haptoglobin frequencies are so different in the Baganda and Bondei and more research on the coastal Bantu might be worthwhile. The possibility of a relationship between malaria endemicity and the incidence of haptoglobin-negatives has been discussed by *Allison* (1959). In Northern Nigerians, *Barnicot, Garlick and Roberts* (1960) found no evidence that the frequency of this phenotype in different age groups corresponded to the age distribution of parasitaemia. Nevertheless the high frequency in the Baganda who live in an endemic area, and in the Bondei, who also inhabit a malarious region, as compared with the Masai, Bushmen and Zulu who inhabit much less malarious parts suggests that there is some connection.

Summary

The haptoglobin and transferrin frequencies of the Baganda and of small samples of Masai and Bondei have been determined and compared with those of other African peoples.

Zusammenfassung

Haptoglobin- und Transferrinhäufigkeiten der Baganda und kleiner Gruppen der Massai und Bondei wurden bestimmt und mit denen anderer afrikanischer Bevölkerungen verglichen.

Résumé

La fréquence des haptoglobulines et transferrines chez les Baganda et chez un petit nombre de Masai et de Bondei a été déterminée et comparée avec celle d'autres peuplades africaines.

Acknowledgements

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HAPTOGLOBIN TYPES IN MACACA IRUS

By LARS BECKMAN and GUNILLA CEDERMARK

1. Introduction

By means of starch gel electrophoresis *O. Smithies* (1955 a and b) demonstrated three different patterns of human serum haptoglobin. *Smithies and Walker* (1955) found that the three groups originally called I, II A and II B were controlled by two autosomal genes without dominance. The groups were later termed Hp 1–1, Hp 2–1 and Hp 2–2 respectively (*Smithies and Walker* 1956). Later investigations from Norway (*Fleischer and Lundevall* 1958), Denmark (*Galatius-Jensen* 1958 a) and Finland (*Mäkelä et al.* 1959) have all confirmed the hypothesis of inheritance proposed by *Smithies and Walker*. Some cases of atypical segregation have, however, been reported by *Harris et al.* (1958).

Allison et al. (1958) reported a high frequency of individuals without serum haptoglobin in Nigerian Africans. Absence of haptoglobin might depend both on genetical factors (cf. *Galatius-Jensen* 1958 b) and environmental factors as haemolytic disease (*Laurell and Nyman* 1957).

Giblett (1959) found about 10 per cent of a modified Hp 2–1 type among American Negroes. The type was described by *Connell and Smithies* (quoted by *Giblett* 1959) who suggested the tentative name Hp 2–1 (mod.). Other modifications of the Hp 2–1 heterozygote have also been observed (cf. *Galatius-Jensen* 1958 b, *and Blumberg et al.* 1959).

Arends and Rodriguez (1960) have examined the sera of 27 monkeys (23 Macaca mulatta, 3 Cebus negrivittatus and 1 Macaca irus). All the monkeys were found to have type Hp 1–1. The authors claimed that if future investigations would confirm that monkeys have only one type of haptoglobin, this might be a phylogenetically significant finding. *Mäkelä et al.* (1960) have examined the sera of 17 Macaca mulatta, 10 Macaca radiata, 1 Papio hamadryas, 1 Cercopithecus aethiops and 2 Pan troglodytes. All were found to have a pattern similar to the human Hp 1–1 type. *Beckman and Cedermark* (1960) have, however, reported the finding of Hp 2–1 heterozygotes in Macaca irus.

2. *Haptoglobin types in Macaca irus*

We have examined the sera of 30 Cynomolgus monkeys (Macaca irus. F. Cuv.) by means of starch gel electrophoresis, using the discontinuous buffer system described by *Poulik* (1957). Haemoglobin from the monkeys was added to the sera prior to electrophoresis. The gels were stained with both amidoblack and benzidine.

Two different patterns were found (cf. fig. 1). Double runs together with human haptoglobin types revealed that the benzidine-staining zones occupied the same electrophoretical position in human and monkey sera. The two types corresponded to the human Hp 1–1 and Hp 2–1 groups. In the Hp 2–1 type of the monkeys the slow-migrating bands are weak, while the band corresponding to the human Hp 1–1 band is very strong. In the photograph (fig.1) only one of the three slow migrating bands of the heterozygote is clearly visible. In fresh benzidine stains usually two, sometimes three bands can be seen. Thus the heterozygote found in monkeys resembles the Hp 2–1 (mod.).

There is a close agreement between the observed and expected frequencies of the different groups (cf. table 1). The frequency of the Hp 1 gene is high (about 90 per cent). It is then quite reasonable that no Hp 2–2 homozygote has emerged, since the expected frequency of this type is only about 1 per cent.

3. *Discussion*

The frequency of the Hp 1 gene in Macaca irus is significantly higher than in Europeans. The distribution is rather similar to that found in African Negroes (*Sutton et al.* 1956). Macaca irus occurs originally in southeast Asia. Human populations from that area are characterized by a very low frequency of the Hp 1 gene (*Kirk et al.* 1960). Thus there seems to be no agreement between human and monkey populations living in the same

(a) Human Hp 2–1

Monkey Hp 2–1

(b) Monkey Hp 1–1

Monkey Hp 2–1

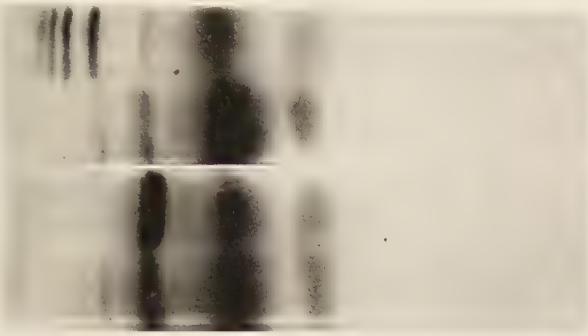

Figure 1

Gels stained with benzidine. (a) Double-run with Hp 2–1 from human and monkey sera. (b) The two haptoglobin types observed in Macaca irus.

Table 1

Frequencies of haptoglobin types in Macaca irus

	Hp 1–1	Hp 2–1	Hp 2–2	n
obs.	23	7	0	30
exp.	23.4	6.2	0.4	30

area concerning the distribution of haptoglobin types. This indicates that there may be differences in the selective value of the haptoglobin types in the human and monkey populations of south-east Asia. It is perhaps worth pointing out that in Negroes, having a similar distribution of haptoglobin types, there is a relatively high frequency of the Hp 2–1 (mod.). *Harris et al.* (1959) have pointed out that Hp 1 gene of the Hp 2–1 mod. does not seem to be peculiar. Thus the modified Hp 2–1 may depend on a special Hp 2 allele which in homozygous condition may have a selective disadvantage.

Summary

The haptoglobin types of 30 Cynomolgus monkeys (Macaca irus) have been examined by means of starch gel electrophoresis. Two types corresponding to the human Hp 1–1 and Hp 2–1 mod. have been observed. The frequency of the Hp 1 gene is very high.

Zusammenfassung

Die Haptoglobin-Typen von 30 Cynomolgus-Affen (Macaca Irus) wurden mit Hilfe der Stärkegelelektrophorese untersucht. Es wurden zwei Typen

beobachtet, die dem menschlichen Hp 1–1 und Hp 2–2 entsprechen. Das Hp 1–1-Gen tritt sehr häufig auf.

Résumé

Les différents types d'haptoglobine ont été examinés chez 30 singes cynomolgus (Macaca irus) par l'électrophorèse au gel d'amidon. Deux types correspondant au Hp 1–1 et Hp 2–1 mod. ont été observés. La fréquence de Hp 1 est particulièrement grande.

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ATROPHIC AND ALBO-PAPULOID DYSTROPHY OF PASINI

A Variant of Epidermolysis bullosa.

By SIMA ILIĆ and DANILO STEVANOVIĆ

Atrophic and albo-papuloid dystrophy (a.a.p.d.) of the skin is a comparatively rare clinical picture. The disorder was first described in 1928 (1) and nowadays regarded as a variant of hyperplastic dystrophic epidermolysis bullosa; small, oval, ivory efflorescences, elevated or in level with the skin, appear usually in the second decade of life in persons who have already been affected with epidermolysis bullosa from early infancy. Only dystrophic nails and scars on the site of former blisters are seen. Other ectodermal growths, such as hair and teeth, are usually not affected. The a.a.p.d. lesions appear chiefly on the trunk independently of blister formation.

Both sexes are equally affected.

The latest extensive report dates from 1956 (2). Genealogical data of this case are scanty. No other member of the family was affected with a similar skin condition, though goiter, observed in the patient – was also found in some other family members both on the father's and mother's side.

Case report

A boy now aged 11, has been seen periodically at the department since the age of six. The patient is the first child born of a healthy mother. The

father, however, has similar skin changes. A second child, a girl, now aged 7 is both physically and mentally normally developed. The mother also had a history of a spontaneous abortion in her second month of pregnancy. According to the mother, the patient was born in the eighth month of pregnancy. His weight at birth was 2700 gram. He began to walk and speak only in his third year.

The patient's father, grand-father and great grand-father (paternal side) had dystrophic nails. The patient's father (individual no. 2 in the pedigree) does not recall whether his grand father (indiv. no. 4) had any blisters. The patient's father and grand father (indiv. no. 3) also had blisters in their youth. Among eleven siblings on the father's side (indiv. nos. 2, 5, 6, 7, 8, 9), only one (no. 9) is alive (besides the patient's father); three died of tuberculosis at the age of 26 (no. 5), 17 (no. 6), and 20 (no. 7). Six siblings (no. 8) died soon after, or within the first year, after birth. The patient's father does not remember whether his brother (no. 5) had any skin changes. In his marriage with a healthy woman there were however, 4 stillbirths (no. 11) and a healthy baby (no. 10). The only other sibling alive (no. 9) besides the patient's father has 4 children. One of these with congenital luxation of the hip (no. 12), had two normal children; another is affected with epidermolysis bullosa hyperplastica (no. 13) and two of his children (nos. 14, 15) have the same condition, another is normal (no. 16) with a healthy child, and yet another has kyphoscoliosis (no. 17).

Protruding ears are found in a son of one of the sisters of the mother.

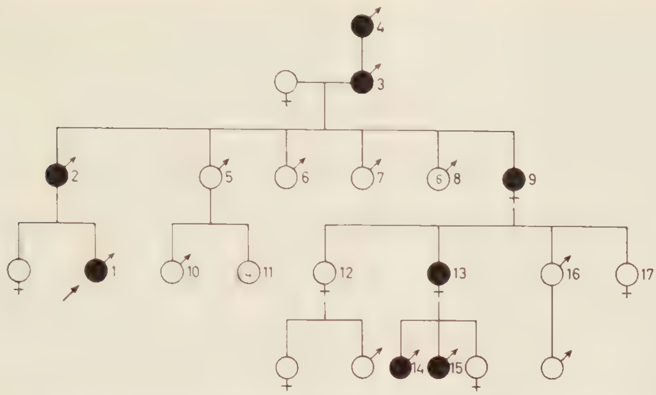
The first blisters in the child appeared about the age of one year subsequent to a trauma; such trauma is usually produced by scratching and according to the mother the pruritus in the child was always intense.

The first lesions of the back appeared round the age of 5. According to the previous objective findings these were then more papular. The mother thinks that these are also the sequelae of scratching and secondary infection of these sites. A few years ago the child burnt himself on the chest (on the edge of a stove). This also resulted in clearly visible scars in the area between the nipples.

Dystrophic toe nails have been present almost since birth; a dystrophic process of the finger nails started later.

On examination two oval scars were seen, one on each knee with milia mainly on their periphery. The scars are brownish in colour and of papery appearence.

On the trunk, anterior and posterior, there are many small and large circular and irregular scars (Fig. 1). In contrast to the lesions on the knees, these scars are mainly whitish in colour; some of them, however, have a



(Chart) Pedigree of a family affected with epidermolysis bullosa hyperplastica dystrophica. (For explanation see text).

Fig. 1. The appearance of the back. There are many white atrophic lesions with cysts on the edge of the larger ones.

definite reddish hue. Some scars show furthermore follicular ostia. Definite cysts are also associated with some of these scars. The mother is certain that these scars were not preceded by blisters. Obvious papular lesions are not present; some of the lesions are, however, slightly elevated.

Between the nipples there are 2 white scars; their upper edge is at the same level. These are the sequelae of the accidental burn mentioned (Fig. 2).

Fig. 2. Note the expression of the face, protruding ears, two longitudinal scars (burns) and many smaller ones on the chest, and two round atrophic scars on the knees – brownish in colour.

The patient's intelligence corresponds to a child aged 4 to 5. In the electroencephalogram the absence of α-rhythm with irregular quicker and slower waves was noticed. A biopsy of an "albo-papuloid" efflorescence showed epidermis at some places slightly invaginated and the follicular orifices enlarged. The keratinous layer is moderately pronounced, penetrating the ostia mentioned. The granular layer is hardly noticeable, and rete pegs are reduced to a few layers of cells. The basal cells are rich in melanin. In a condensed dermis a hypertrophy of the sweat glands and their excretory canals is visible.

A section through a blister showed the epidermis to be slightly hyperkeratotic and atrophic with the rete ridges flattened. The blister is subepidermal. Cysts and hypertrophic sweat glands are visible in the dermis.

The chemical analysis of the blood was within normal limits. Serologic

tests for syphilis were negative. Routine laboratory analyses did not reveal anything abnormal.

Discussion

A mainly dominant inheritance was observed in the albo-papuloid variant of epidermolysis bullosa. A recessive inheritance has been mentioned, among others, by *Cerutti, Pasini and Bertacini*. The elements both of albo-papuloid and ulcero-vegetating type were found in *Leinbrock*'s (2) patient. The former variant is usually inherited as a dominant, and the latter as a recessive characteristic.

The isolated occurrence of epidermolysis bullosa, and a.a.p.d., in different members of the same family was recorded by *Touraine* (3). The same observation was made in the family of the patient described in this paper.

Electroencephalographic findings of epilepsy and petit mal were already described in patients with a.a.p.d. by *Wende* (4), and by *Kissel* (5), the latter also found electroencephalographic changes in members of two families with no skin lesions, but who belonged to the families with epidermolysis bullosa (dystrophic). Imbecility is usually reported as being associated with malignant forms of dystrophic epidermolysis bullosa in whom life span is usually short. To our knowledge our case is the first one in which imbecility occurred both in a.a.p.d., and in hyperplastic epidermolysis bullosa.

The inherited disorders of the spine are of minor significance among genetically determined diseases. The familial occurrence of scoliosis and other forms of spine deformities does not seem, however, to be rare. *Faber* (6) reports 174 familial cases, where inheritance was regularly or irregularly dominant. The sister of the patient with scoliosis had congenital luxation of the hip, which is also accepted by some authors as an inherited anomaly, both dominant and recessive. *Pfändler* (7) assumes a common genetic factor for hip and knee malformations. Such a genetic factor is possibly an explanation of the occurrence of two different anomalies of the great bones in two sisters belonging to a family affected with epidermolysis bullosa. Bones are of mesodermal origin, while tissues affected in epidermolysis bullosa are of ectodermal origin (skin, brain).

Protruding ears are a common occurrence in some races such as the Kabyles, the Kalmouks and the Turcowers. According to *Leicher* (8), this anomaly is inherited as a recessive. Since no known member on the father's side of our patient had this anomaly, and only one (no. 18) member on the mother's side had such a condition, such an inheritance may be also possible in our patient.

An unusual finding is the occurrence of cysts on some "albo-atrophic" efflorescences; this could however be expected, since cysts can also be found in some other skin conditions, not directly related to epidermolysis bullosa.

In our patient an accidental burn resulted in a scar similar in appearence

to other lesions on the trunk; this may suggest a similar reaction of the skin in patients with albo-papuloid lesions to different irritations.

The various malformations occurring in our family can not be regarded as depending on the same gene. Bone malformations which are of mesodermal origin are probably attributable to one gene, independent of the gene which conditioned epidermolysis bullosa. Complete dihybridism, however, was not encountered in our family, since malformations produced by these two genes were not seen in one and the same person.

The imbecility and the epidermolysis bullosa encountered in the patient are closely related and can be regarded as belonging to a true hereditary chain in *Touraine*'s sense and the patient as affected with a neuro-ectodermal genodermatose.

Stillbirths and early death within three months from birth are seen in families affected with epidermolysis bullosa dystrophica. A similar lethal factor must also be assumed to be the cause of stillbirth occurring in some members of this family. There was no information concerning the condition of the skin of the stillborns; it is, however, known, that early death of offsprings in such families can also occur without evident skin changes suggesting epidermolysis bullosa (9).

Summary

A case of hyperplastic epidermolysis bullosa of the albo-atrophic type is reported. Imbecility in the patient, and certain genetically determined malformations in some other family members were the main findings.

Zusammenfassung

Über einen Fall von hyperplastischer Epidermolysis bullosa des alboatrophischen Typs wird berichtet. Die Hauptbefunde waren Imbezillität beim Patienten sowie gewisse genetisch bedingte Mißbildungen bei einigen anderen Familienmitgliedern.

Résumé

Les auteurs décrivent un cas d'épidermolysis bullosa hyperplastique du type albo-atrophique. Ils soulignent que le malade présente en outre une imbécillité et qu'on trouve dans la famille d'autres malformations d'origine génétique.

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MULTIPLE SCLEROSIS IN TWINS AND THEIR RELATIVES:

GENETIC ANALYSIS OF FAMILY HISTORIES[1]

By N. C. MYRIANTHOPOULOS and R. P. MACKAY

Mackay and Myrianthopoulos recently (1958) presented preliminary findings of a genetic and clinical study of multiple sclerosis in 54 pairs of twins and over one thousand of their relatives. The methods of collection of the twin sample and the family histories, and the methods and criteria employed in the clinical and genetic evaluation of the data are described in the above mentioned report. The object of this report is to present a genetic analysis of the family histories involving 1,112 relatives of the twin cases.

In summary, the twin sample consisted of 54 pairs of twins, 29 monozygotic and 25 dizygotic. At least one member of each pair had multiple

[1] This investigation was supported by Grant No. 87 from the National Multiple Sclerosis Society.

sclerosis at the beginning of the study. The difference in concordance rate between the monozygotic and dizygotic twin pairs was interpreted as not significant and thus not constituting conclusive evidence that genetic factors operated in the causation of the disease. It was emphasized, however, that the figures obtained were lessened by several important limiting factors. Chief among these was the bias which entered in the selection of the twin sample. This was well reflected in the departure of the sample from the expected zygosity and sex distribution.

The particular selection bias involved in obtaining the twin sample does not apply to the study of the relatives. These are a series of persons who were brought into the study because they had some specified relationship with the propositus. The results of the study of the relatives, therefore, may be more illuminating than those of the twin study.

The propositi are defined as follows: In the case of monozygotic twins, both twins in the twinship are considered as *one* propositus since they are isogenic. In the case of dizygotic twins, however, only the index case is considered as propositus since the twins are genetically different, as are ordinary siblings. The co-twins of dizygotic propositi, therefore, have been counted as siblings. A breakdown of the various relationships investigated and their response is given in Table 1. No consanguineous marriages were found among the parents of the propositi but one case of first cousin marriage among the grandparents came to our attention.

The occurrence of multiple sclerosis among the relatives is given in Table 2. The relationship "first cousins once removed" was not investigated during the course of this study. The one affected relative in this relationship was reported to be a first cousin although later, when the family

Table 1. Relatives investigated

Relationship	Investigated	Responded	% Responded
Parents	62	62	100.00
Siblings	204	182	89.12
Children	57	49	85.96
First cousins	663	519	78.28
Nephews and nieces	126	109	86.50
Total	1.112	921	82.82

From *Mackay* and *Myrianthopoulos*, 1958.

Table 2. Relatives with multiple sclerosis

Relationship	Definite M. S.	Possible M. S.	Total
Parents	1	0	1
Ordinary siblings	4	4	8
Fraternal co-twins	1	3	4
Children	1	0	1
First cousins	3	0	3
First cousins once removed	1	0	1
Total	11	7	18

From *Mackay and Myrianthopoulos*, 1958

history was taken down completely, he was found to be a first cousin once removed. He is not included in the genetic analysis.

Of the 18 affected relatives, nine were males and nine females. The 11 cases of definite multiple sclerosis were distributed among nine families or in 16.67 per cent of the families. The 18 cases of definite and possible multiple sclerosis were distributed among 12 families, or in 22.23 per cent of the families. A comparison of the prevalence of multiple sclerosis in the relatives of the twin cases with the prevalence rate of the disease in the general population and with that reported by others investigating the possible influence of heredity in multiple sclerosis is made in Table 3.

It is necessary here to point out that the figure one in 2,000 which was chosen as being the most representative prevalence rate of the disease in the United States and Canada was derived from the survey-type studies conducted by *Kurland and his associates* (1954 summary). While this figure agrees with those found in other survey-type studies in the United States and abroad, it may be argued that it is not strictly applicable to our material which was collected by a different and, perhaps, more thorough procedure.

While it may be true that in this study some cases were obtained that could not be uncovered by survey-type methods, a more or less equal number of cases reportedly having multiple sclerosis, which might otherwise have been accepted, were rejected as either not meeting the diagnostic criteria or having some other neurological disease. It is felt, therefore, that the reported prevalence rate has not been appreciably altered by the methods and diagnostic procedures employed and that the use in this study of 1 in 2,000 as the prevalence rate of the disease is justified.

Table 3. Multiple sclerosis in relatives: Comparison of data from this study with population prevalence rate and data from other studies

Relationship	Data this study			*Pratt et al.* (1951)	*Müller* (1953)	*Millar and Allison* (1954)
	Prevalence	Per Cent	Times Population Prevalence 1:2000			
Parents	1 in 62	1.6	32.26	1 in 200	1 in 300	
Siblings	1 in 41[1] to 1 in 17	2.45 to 5.88	48.78 to 117.65	1 in 100	1 in 100	1 in 100
Children	1 in 57	1.75	35.08			
First cousins	1 in 166	0.6	12.05			
Total Relatives	1 in 101 to 1 in 62	0.99 to 1.62	20.0 to 32.26		1 in 167	
Family History	1 in 6 to 1 in 4 families	16.67 to 22.23		6.5%	3.6%	6.6%

From *Mackay and Myrianthopoulos*, 1958

[1] First figure is for definite M.S. only. Second figure is for definite and possible M.S. combined

The prevalence of multiple sclerosis in the overall relatives of the twin cases is from 20 to 32 times higher than the prevalence rate of the disease in the general population and the prevalence in the various groups of relatives taken separately ranges from 12 to 117 times higher than the population prevalence rate. Where two figures are given the first figure for each group refers to definite multiple sclerosis while the second figure refers to definite and possible multiple sclerosis combined. The prevalence and percentage figures and the resulting multiple of the population prevalence figures pertain to the total relatives investigated in each group and not only to the number who responded. These figures, therefore, may be an underestimate.

No doubt, both known and unknown biases tend to raise the observed rates over the prevalence rates. Chief among the known ones would be the bias which makes it more likely to observe a second case in the family because of a first one being observed. It would be futile, however, to try and evaluate them precisely. It is sufficient to say that, apparently, the known biases do not explain the observed higher prevalence of the disease among the siblings and, perhaps, among the other relatives. There is still evidence for a familial occurrence of multiple sclerosis and this should be further investigated.

This familial occurrence may be due to either some environmental stress common in the families or to a genetic factor or both. Many theories have been advanced in the past to account for the environmental origin of multiple sclerosis (inflammatory, allergic, infectious, etc.). None of them has been borne out by the facts. The present authors reported in their previously-mentioned publication that they were unable to find any association between multiple sclerosis and birth order within a twinship, birth order within a sibship, occupation, socioeconomic status, nationality background, religious affiliation, general activities or dietary habits.

Failure to find an environmental factor as causative of multiple sclerosis does not mean that such a factor does not exist. The inconclusive findings of twin studies, the peculiar geographic distribution of the disease and the consistent observations of secondary cases which do not seem to segregate in accordance with any simple mode of inheritance, all suggest that environmental factors do play a significant role in the etiology of multiple sclerosis. The available evidence for genetic determination of the disease, although suggestive, is still unclear. A genetic analysis has, therefore, been undertaken to determine whether genetic factors of appreciable magnitude in the etiology of multiple sclerosis can be demonstrated.

Genetic analysis

The method of collection of the histories of the relatives and the completeness of information obtained make these data amenable to genetic analysis for the purpose of testing possible modes of inheritance and the penetrance level at which they operate. It is apparent that the data, complicated by the late and variable age of onset of the disease do not approach sufficiently any of the common genetic ratios to afford a clue for direct analysis. A convenient way of proceeding, therefore, would be to formulate *a priori* hypotheses for simple modes of inheritance and then examine them by an appropriate method.

In the twin sample there was an excess of females over males and among the affected relatives the ratio of females to males was 1:1. Among the affected siblings there were 5 females and 7 males, a non-significant departure from the 1:1 ratio, considering the smallness of the sample. The hypothesis of recessive sex-linkage, therefore, can be ruled out unless it is assumed that the penetrance is much lower in the males than in the females. Now, the ratio of the sex-linked recessive genotype in males and females is $1:q$. If q^2 is taken as 0.0005, the value of q becomes 0.0224 which makes the genotypic ratio one female to 50 males. For the observed 1:1

ratio the penetrance in the males must be reduced to 2 per cent, which is absurd. Furthermore, there were two cases of female to female transmission in the sample (one, parent to index case and one, index case to daughter) which tend to rule out recessive sex-linkage.

It is very unlikely that the trait is sex-linked dominant and the argument against this hypothesis is the same as that used immediately below to rule out dominant inheritance. It is interesting to note that in all instances in which a secondary case was found, the index case was a female. This can presumably be explained by the preponderance of females in the twin sample.

Autosomal dominance can be ruled out easily because of too few affected parents. The level of penetrance necessary for this hypothesis is also absurdly low. Figuring roughly, of the 102 parents, at least half must have had the dominant gene but only one was affected so that the penetrance must have been less than 2 per cent. There were 226 siblings other than the propositi, and if half of them were expected to have the genotype, the 2 per cent penetrance would result in an expected 2.26 affected siblings, a significant deviation from the 12 observed.

Of the simple modes of inheritance there remains the autosomal recessive hypothesis, and this appears to be the most likely one especially because of the virtual absence of affected parents. The lack of consanguinity among the parents may make the recessive hypothesis doubtful (although one case of first cousin marriage was found among the grandparents) but this may be due to the smallness of the sample. Other investigators reported consanguinity among parents of patients with multiple sclerosis. *Curtius* (1959) summarized first-cousin marriage rates from his data and those of *Bell*, and *Pratt and his associates* and found that these were significantly higher than would be expected by chance in the respective populations of Germany and England.

If the recessive hypothesis is accepted *a priori*, the analysis may proceed in two steps. First, it may be decided whether the trait is fully penetrant; and if not (as it appears from a cursory examination of the data) some estimate of penetrance may be derived by comparison of the affected expected to the observed. Second, this estimate of penetrance may be used to examine the observed data for other affected relatives, namely parents, children and first cousins.

In selecting an appropriate method for estimating penetrance and testing the hypothesis it is essential to keep in mind that the disease has a late and variable age of onset. A very useful method providing for the necessary age correction has been developed by *Pincus and White* (1933). This

method is based on the reasonable assumptions that the survival rate of individuals not affected with a certain disease (in this case multiple sclerosis), but genetically liable, is not different from that in the general population, and that the distribution of age of onset of the disease in the patients' siblings is representative of the age of onset in the general population.

Since the *Pincus and White* method has been designed to compare the expected prevalence of the disease in the siblings with the observed prevalence, only families with more than one child can be used in the calculations. There were 51 such families in the sample. Also, since the hypothesis to be tested is a recessive hypothesis it is assumed that the mating type of the parents is *MSms* × *MSms* in which case neither of the parents would be affected. Excluding the one family with one affected parent (of presumed mating type *MSms* × *msms*) there remain 50 families with 275 siblings. This number includes all the known siblings, that is, even those who have not cooperated in the study and those who are deceased.

Two main corrections have to be made in the course of the analysis, the first for family size and the second for the late and variable onset of the disease.

The first correction, for family size, accounts for the fact that in a recessive condition with complete penetrance something more than the Mendelian ratio of one affected sibling in four is expected, since each of the families was chosen because at least one affected child was identified. The Mendelian expectation of *msms* children is given by:

$$\frac{p}{1 - q^n}$$

where p is the probability of an *msms* individual appearing, q the probability of an *msms* individual not appearing and n the number of children per family. For example, in an *MSms* × *MSms* mating with six children, the expectation of *msms* individuals is:

$$\frac{1/4}{1 - (3/4)^6} = 30.41 \text{ per cent}$$

There were 11 six-child families in our sample with a total of 66 children and 30.41 per cent of them, 20.06 children, are expected to have multiple sclerosis. These were of various ages up to 70 and so far 11 of them (the propositi) had developed the disease. This leaves 9.06 *msms* children still potential multiple sclerotics who had not shown evidence of the disease at the time of this study. These are distributed among the various age groups – ten year groups in these calculations – proportionally to the number of children in each age group. Thus, the expectation of potential multiple

Table 4. The expected and observed prevalence of multiple sclerosis in siblings of propositi when neither parent was affected

1 Decade	2 Affected expected after correction for family size	3 Affected observed *(Mackay and Millar)*	4 % affected observed	5 % surviving decade (U.S. pop. 1939–1941)	6 Potential not identified each decade	7 % potential identifiable	8 Expected number identifiable (2 × 7)	9 Number affected this study
0– 9	1.72	1	0.14	94.33	106.59	0.13	0.00	0
10–19	1.92	67	9.31	98.90	96.11	8.83	0.17	0
20–29	3.57	239	33.19	97.99	60.99	35.24	1.26	1
30–39	10.45	261	36.25	97.02	22.93	61.25	6.40	3
40–49	10.59	131	18.19	94.28	3.43	84.13	8.91	3
50–59	5.97	19	2.64	87.80	0.37	87.71	5.23	4
60–69	3.49	2	0.28	74.84	0.00	100.00	3.49	0
Totals	37.71	720	100.00				25.46	11

sclerotics in each family size is calculated and summed up for each decade of life. The expected figures are shown in column 2 of Table 4. The propositi are omitted from the tabulation and only the actual and potential multiple sclerotics among the siblings of the propositi are included in the expected figures.

The second correction accounts for the fact that because multiple sclerosis has a late and variable age of onset, the frequencies observed are lower than they would be if all individuals in the sample had reached, say, age 70, which is the assumed age at which all potential multiple sclerotics would be identified.

For this correction, information is required from the two sources: first, from life expectancy tables to show how many people who start a decade of life survive to the end of the decade. This was obtained from life expectancy tables of the United States white population for the years 1939–1941 (*Dublin et al.*, 1949). Second, from reliable data showing the frequency of onset of multiple sclerosis for each decade of life. These were obtained by combining the data published by *Mackay* (1953) and *Millar and Allison* (1954) comprising 720 cases. These data are shown in columns 3 and 5 of Table 4. It is assumed here that the population at risk in the *Mackay*, and *Millar and Allison* data is subject to the same death rates as those of the U.S. white population. This assumption presents no difficulty.

It will be noticed that of the 720 cases only 0.28 per cent began in the 60–69 decade. But only 74.84 per cent of the 60–69 year olds survived all

the way through the decade and the 0.28 per cent observed do not represent all the potential multiple sclerotics available in the 50–59 year population. The total of potential non-surviving multiple sclerotics for the 50–59 year range are calculated and added to the observed in column 4. For each preceding decade the same procedure is repeated until the potential multiple sclerotics not identified in each decade of life are calculated, as shown in column 6 of Table 4. It is assumed, of course, that all potential multiple sclerotics can be identified as affected by age 70. (Columns 5 and 6 of Table 4 have a couple of compensating errors in their make-up and use. For example, the 2 cases in column 3 in the 60–69 decade represent more than 74.8 per cent of the experience of the 50–59 year olds. That would be the case if they all died at age 60 instead of throughout the decade from 60–69. If adjustment for this is made the resulting values are not different from those given. This is because the two corrections tend to be in the opposite directions. See later, in the discussion.) The proportion of the total identifiable in each decade of life is next calculated from columns 4 and 6 by working upwards and is given in column 7 of Table 4.

The expected number of affected siblings identifiable in each decade of life can now be obtained by multiplying column 2 by column 7 of Table 4. The product is shown in column 8 and can be compared with column 9 which gives the number of affected siblings from this sample.

The expected number of affected siblings is 25.46 while the observed number is 11. A sum of chi-squares test for the extent of agreement of expected with observed affected siblings, shown in Table 5, yields the figure 11.13. With six degrees of freedom, $0.1 > P > 0.05$ is not significant at the 0.05 level (the 0–9 decade is excluded because, since expected and observed were both zero, the comparison would merely inflate the degrees of freedom). In the last column of Table 5 the individual chi-squares were corrected with the *Yates* correction to test if there were any significant differences between the expected and the observed affected siblings in each age group. None of the individual corrected chi-squares is significant at the 0.05 level. It should be noted, however, that the deviations of the observed from the expected are always in the same direction, i.e., the observed affected siblings in each age group are less than the expected, except in the 0–9 decade where both are zero. The probability of this occurring by chance is $(1/2)^6$ or $1/64$ and the probability of this good fit or worse is $1/32$ which is a significant departure from expectation at the 0.05 level.

A more meaningful test, therefore, would be one on the combined data. The chi-square on the combined data is 8.82 and $0.01 > P > 0.001$. This

Table 5. Chi-square tests for extent of agreement between expected and observed numbers of affected siblings under the recessive hypothesis

Decade	Number of Siblings	Observed	Expected	Uncorrected χ^2	χ^2's with the *Yates* correction
0– 9	10	0	0	0	0
10–19	12	0	0.17	0.173	0.007
20–29	22	1	1.26	0.057	0.049
30–39	62	3	6.40	2.016	1.467
40–49	63	3	8.91	4.563	3.824
50–59	35	4	5.23	0.340	0.120
60–69	21	0	3.49	4.184	3.071
Totals	225	11	25.46	11.333	

[1] Sum of the uncorrected chi-squares: $\chi_6^2 =$ 11.33
$0.10 > P > 0.05$

[2] Individual (corrected) chi-squares: None is significant at the 0.05 level.

[3] Chi-square on the combined data: $\chi_1^2 =$ 8.82
$0.01 > P > 0.001$

means that the data taken as a whole differ significantly from expectation under the null hypothesis. The reason for the difference between the sum of chi-squares and the chi-square on the combined data is that the latter reflects the consistent direction of the deviations from decade to decade. The alternative to the null hypothesis for the chi-square on the combined data is that each or all observed are less than the corresponding expected. This is an important point in the reasoning, for if on the basis of the chi-square on the combined data the null hypothesis is rejected and the alternative one accepted, as it is, then the differences between observed and expected affected can be ascribed to reduced penetrance of the homozygous recessive genotype.

The penetrance of the recessive gene is estimated by dividing the observed number of affected siblings (column 9 of Table 4) by the expected number identifiable (column 8 of Table 4), in this case 11/25.46, or 43.2 per cent.

The recessive hypothesis can now be tested by estimating the expected number of other affected relatives and comparing it with the observed number, using the penetrance figure of 43.2 per cent.

There were three affected first cousins among the relatives of the twin cases. One of these affected cousins was found among the relatives of the

twinship with one affected parent and is, therefore, excluded from these calculations.

Since it is assumed that the mating type of the parents of the propositi is *MSms* × *MSms*, the chance that a sibling of either of the parents will carry the recessive gene is $^1/_2$. The chance, now, that the spouse of such a sibling (aunt or uncle of the propositus) will also carry the gene is a function of the frequency of the gene in the general population. It will be recalled that the prevalence rate of multiple sclerosis was taken to be 1:2000 population, or $q^2 = 0.0005$. If, however, the gene has only 43.2 per cent penetrance, this value of q^2 represents only 43.2 per cent of the people who are homozygous for this gene. The value of q^2 for 100 per cent of homozygous recessive people is 0.0012. Then, $q = 0.0346$, $p = 0.9654$ and $2pq$ becomes 0.0668. In other words, one out of about 15 persons in the population is heterozygous for the *ms* gene. The chances, therefore, that a first cousin of an affected person will likewise be affected are $^1/_2 \times {}^1/_{15} \times {}^1/_4 = {}^1/_{120}$. Among the 499 first cousins of the 50 twin cases, then, 0.84 per cent are expected to be affected. This estimate, of course, is based on the assumption that the gene has full penetrance. Since the gene was found to have only 43.2 per cent penetrance, the frequency of affected first cousins in the sample becomes 0.36 per cent or 1.79 individuals. Actually, two affected first cousins were observed. The agreement between expected and observed affected first cousins is evidently very good.

The expectation of affected cousins, for all types of matings which can produce homozygous recessives, can be estimated directly by using the formula

$$P \frac{q\,(1+3q)}{4}$$

where P is the penetrance and q the true frequency of the recessive gene. In this case if $P = 0.432$ and $q = 0.0346$, the expectation of affected first cousins among the 519 first cousins of 51 twin cases is 2.13, which again is in good agreement with the three observed.

The expectation of affected parents and children can also be estimated using the derived penetrance figure. This is given by Pq (applicable to both parents and children). The expected figures in this case are 0.92 for parents and 0.85 for children, which are in good agreement with the one parent and one child observed.

From the foregoing it appears that the hypothesis of a pair of recessive genes with 43.2 per cent penetrance could well explain the data.

Discussion

The problems confronting the geneticist who attempts an analysis of complex data such as those presented here, were succinctly summarized by *Neel and Schull*, who wrote: "There are diseases with a hereditary element in whose study one may encounter all three of these statistical problems, i.e., incomplete penetrance, a variable age of onset and an uncertain degree of ascertainment. In addition, the possibility that the disease is genetically heterogeneous hangs constantly over the investigator's head. . . . The genetic approach to a collection of medical data can, on occasion, contribute importantly to clarifying clinical concepts. On the other hand, there are times when the proper genetic analysis of a given disease must await certain medical advances."

The present authors are, indeed, in full agreement with this statement. But they chose to be optimistic in their belief that an earnest attempt, however beset by the limitations mentioned above, might contribute to the understanding of the etiology of multiple sclerosis and encourage further and better approaches to the problem.

Although the analysis showed that the data are compatible with the hypothesis of a pair of autosomal recessive genes with reduced penetrance, such hypothesis should not be taken as proven. It must be remembered that the hypothesis was made as an *a priori* assumption and then collateral evidence was sought which appeared to agree with a certain estimate of penetrance under the hypothesis. This is, of course, a legitimate procedure, but it may represent only one of many possible solutions and perhaps not the right one.

An analysis of the data was also done by life table procedure with two causes for depletion of the cohort, death and disease. A description of this procedure, which is too lengthy and complex to reproduce here, can be found in *Anderson and Dow* (1952). A correction was introduced in this analysis by taking the 10-year-intervals at mid-point. The results were identical to those obtained by the *Pincus* and *White* method. The excellent agreement of the results obtained by the two methods demonstrates that the errors pointed out earlier in columns 5 and 6, Table 4, of the *Pincus* and *White* method are almost completely compensating.

It must be recognized that the inherent mechanics of the *Pincus* and *White* method—and the double depletion procedure for that matter—correct for the effects of age variation only. Any environmental factors which may inhibit or otherwise affect the expression of multiple sclerosis and which at present are unknown are not accounted for by the method.

From the foregoing it seems reasonable to accept that genetic factors of considerable magnitude operate in the etiology of multiple sclerosis—most likely a pair of autosomal recessive genes—but these are subject to powerful environmental influences which, in fact, have the upper hand. The nature of these environmental stresses and their mode of operation continue do elude our understanding. One finding, however seems to emerge constantly from epidemiologic studies of multiple sclerosis in the United States and elsewhere. *Kurland* (1954 summary) and others have shown that multiple sclerosis is more prevalent in cold and northern climates than in warm and southern ones. One—but not the only—explanation for this could be that there is a correlation between penetrance and the geographic distribution in multiple sclerosis, the warmer climates exerting an inhibitory effect on the genetic action in those individuals who have the genotype. Unfortunately our present sample is too small to test this hypothesis.

The authors plan to follow-up the twins and their relatives in five years. This will make possible a better evaluation of the concordance rate of the twins and a comparison of new cases arising among relatives with theoretical expectations, taking into account the age of onset, under the recessive hypothesis.

Summary

1. Reference is made to the preliminary findings of a genetic and clinical study of multiple sclerosis in 54 pairs of twins and their relatives conducted by the authors. The results of the twin study did not permit any inferences as to whether multiple sclerosis occurred more frequently among monozygotic twins than among dizygotic twins.

2. The study of 1,112 relatives of the twin cases suggests that hereditary factors operate in the etiology of multiple sclerosis. Depending on the rigidity of diagnostic standards 0.99 to 1.62 per cent of the relatives investigated are found to have multiple sclerosis. This is 20.0 to 32.26 times higher than the prevalence rate of the disease in the general population.

3. The expected frequency of multiple sclerosis among the siblings of the twin cases is compared to the observed frequency by the *Pincus* and *White* method. The results are compatible with the hypothesis that multiple sclerosis is determined by a pair of autosomal recessive genes with about 43 per cent penetrance but this hypothesis must not be taken as proven or as the only one that could explain the data.

4. The possible roles of hereditary and environmental factors in the causation of multiple sclerosis are discussed.

Zusammenfassung

Es wird über die bisherigen Ergebnisse einer von den Autoren durchgeführten klinischen und genetischen Untersuchung der multiplen Sklerose an 54 Zwillingspaaren und ihren Verwandten berichtet. Aus den Untersuchungsergebnissen ist nicht zu erkennen, ob die multiple Sklerose bei EZ häufiger als bei ZZ auftritt.

Die Untersuchung von 1112 Verwandten der Zwillingspaare führt zu der Annahme, daß bei der Ätiologie der multiplen Sklerose erbliche Faktoren eine Rolle spielen. Je nach der Genauigkeit der diagnostischen Methoden zeigt sich bei etwa 0,99 bis 1,62% der untersuchten Verwandten eine multiple Sklerose. Das ist 20,0 bis 32,26mal öfter als die zu erwartende Häufigkeit der Krankheit in der Bevölkerung.

Mit Hilfe der Pincus-White-Methode wird die erwartete Häufigkeit der multiplen Sklerose unter den Verwandten der Zwillingspaare mit der beobachteten Häufigkeit verglichen. Die Ergebnisse bestätigen die Hypothese, daß multiple Sklerose von einem Paar autosomal rezessiver Gene mit etwa 43% Penetranz bestimmt wird. Diese Hypothese ist jedoch nicht bewiesen und stellt auch keineswegs die einzige Beweismöglichkeit dar.

Die mögliche Bedeutung erblicher und Umweltfaktoren bei der Auslösung multipler Sklerose wird diskutiert.

Résumé

Il s'agit d'une étude génétique et clinique des constatations préliminaires faites chez 54 paires de jumeaux atteints de sclérose en plaques et chez leur famille respective. Les résultats de l'étude gemellaire n'a pas permis de constater une différence de la fréquence de la sclérose en plaques chez les jumeaux uni- et bivitellins.

L'examen de 1112 personnes apparentées à ces jumeaux parle en faveur de facteurs héréditaires dans la sclérose multiloculaire. Selon la rigueur du diagnostic, 0,99 à 1,62% des personnes examinées montraient une sclérose en plaques. Ceci est 20,0 à 32,26 fois plus que la fréquence de la maladie dans la population.

La fréquence prévue pour les frères et sœurs atteints a été comparée avec la fréquence statistique selon la méthode de *Pincus et White*. Les résultats concordent avec la théorie que la sclérose en plaques est due à un gène autosomal récessif avec une pénétrance de 43% dans l'état homozygote.

Toutefois cette théorie n'est pas prouvée, mais c'est la seule pour le moment qui explique le résultat obtenu.

Les rôles possibles de l'hérédité et des facteurs péristatiques dans l'étiologie de la sclérose en plaques sont discutés.

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A NEW GROUP-SPECIFIC SERUM SYSTEM (GC-GROUPS) IN RELATION TO BLOOD AND SERUM GROUPS

By JAN HIRSCHFELD and LARS BECKMAN

1. Introduction

The immuno-electrophoretic technique, originally described by *Grabar and Williams* (1953) is a combination of electrophoresis in agar-gel and a precipitin reaction in the gel between the electrophoretically separated serum components and their corresponding antibodies obtained by immunisation of *e.g.* rabbits with human serum.

After electrophoretic separation of the human serum, the immune serum is added in a basin longitudinal with the electrophoretic migration axis and situated at a certain distance from the electrophoretically separated antigens. Diffusion of antigen and antibodies towards each other under ideal circumstances give rise to arc-shaped precipitates in the gel, which might have different electrophoretic positions, diffusion positions and shapes. The electrophoretic position of a precipitate indicates the electrophoretic position of its corresponding antigen, the diffusion position is indicative of the diffusibility of the antigen in relation to the diffusibility of its antibody and the shape of the precipitate indicates the electrophoretic distribution of closely situated antigens, which are immunologically identical although occupying different electrophoretic positions (cf. *Grabar*, 1958 and *Hirschfeld*, 1960 a).

In the present study immuno-electrophoresis was carried out on object slides according to *Scheidegger* (1955) with some further modifications (*Hirschfeld*, 1959 a and b). A total of 25 different precipitates have been defined according to electrophoretic position, site between diffusion centres and shape of the precipitate (*Hirschfeld* 1960 b).

These components have all been found in a single evidently normal serum when tested against selected immune sera prepared on rabbits.

The immuno-electrophoretic pattern is remarkably constant when different normal sera are investigated. Two of the 25 precipitates, both situated in the α_2-globulin region under the experimental conditions employed, have, however, been found to occupy clearly different electrophoretic positions, diffusion positions and shape of the precipitates, when different normal sera are investigated.

It is thus possible to demonstrate 2 immunologically distinct group specific systems, each of them allowing a further grouping of human sera into three qualitatively different types, which appear constant for the same individual.

One of these systems has been found to be identical with the earlier by means of starch-gel electrophoresis demonstrated haptoglobin groups (*Smithies* 1955) which have also been found to be genetically determined (*Smithies and Walker* 1955). Also in immuno-electrophoresis the haptoglobins present variations in electrophoretic position, so that the Hp 1–1 type is faster migrating than Hp 2–2, whereas Hp 2–1 occupies an intermediary electrophoretic position (*Hirschfeld* 1959 b, 1960 b).

The other of these systems has hitherto only been demonstrated by means of immuno-electrophoresis (*Hirschfeld* 1959 b), and also in this instance evidence has been put forward for a genetical mechanism (*Hirschfeld, Jonsson and Rasmuson* 1960 d).

In this system, also three different serum types may be distinguished; sera of type 1 and 3 are characterized by a fast respectively a slow moving precipitating component, which both give normally arc-shaped precipitates occupying the same diffusion positions, whereas sera belonging to group 2 give a single precipitate with two peaks, the two peaks occupying the same electrophoretic position as the fast and slow moving precipitating components found in certain other sera (*Hirschfeld* 1959 b).

A mixture of sera belonging to type 1 and 3 in equal amounts in immuno-electrophoresis gives a precipitate with two peaks which is indistinguishable from the two-peaked precipitate found in certain unmixed sera (*Hirschfeld* 1959 b and 1960 a).

The two-peaked precipitate indicates that the components giving rise

to this precipitate are immunologically identical although electrophoretically different. The immunological identity of these components has also been further confirmed by absorption experiments (*Hirschfeld* 1960 c).

The three serum types are probably determined by two autosomal alleles without dominance. From genetical studies it appears that types 1 and 3 are homozygotes and type 2 the heterozygote (*Hirschfeld, Jonsson and Rasmuson* 1960 d).

The mixture experiments as well as genetical studies suggest that two electrophoretically different although immunologically identical precipitating components exist in human sera, which might occur together in approximately the same amounts in certain sera or alone in certain other sera. The fast moving component has been called groupspecific component 1 (G.c. 1), the slow moving component group-specific component 2 (G.c. 2).

In analogy with the notation for the haptoglobin groups, we now suggest the notation Gc^1 and Gc^2 for the genes and Gc 1–1, Gc 2–1 and Gc 2–2 for the serum types "fast", "two-peaked" and "slow".

The nature of these serum components is at present unknown. The diffusion position of these components is close to the antibody diffusion centre, which is at least suggestive of low molecular weight compounds, but they do not penetrate a dialysis membrane. Should they in the future be further identified with previously described serum components it might be advisable to change the locus symbol to some other more descriptive term.

2. Gc-groups in relation to blood and serum groups

The A_1, A_2, B, 0, Rh, MN and P blood groups of 122 unrelated healthy women were determined together with the Gc-groups. Kell-data were available only for 118 children.

As appears from the observed distributions in table 1, the Gc-groups seem to be independent of the blood groups investigated with the exception of the P-system, where a significant association ($\chi^2 = 7.90$, 1 d.f., $P \sim 0.005$) is found. In the analysis the Gc 2–1 and Gc 2–2 groups were taken together.

As the individuals in this report are mothers examined in medico-legal connections it was possible to obtain data on the relation between the P– and Gc-groups also for their children (table 2). No significant association was found in this sample ($\chi^2 = 0.56$, 1 d.f., $0.5 > P > 0.3$).

It is known that the strength of the P-antigen is considerably weaker in children, and the more unreliable determination of this system in children as compared to adults might affect the results (cf. *Race and Sanger*, 1958).

On account of the discrepant results between the two samples no definite conclusions can be drawn until further results have been obtained.

The haptoglobin groups for 102 adult individuals were determined by starch-gel electrophoresis using a discontinuous buffer system (*Poulik* 1957). No significant association between haptoglobin groups and Gc-groups was found (table 3).

It was also found that the Gc-groups were not identical with the transferrins, the Gm groups or the cholin-esterase groups (*Kalow et al.* 1957).

Table 1

Gc-groups in relation to blood groups

	Gc 1–1	Gc 2–1	Gc 2–2
A_1	26	19	2
A_2	2	7	0
B	7	5	0
A_1B	4	2	0
A_2B	0	0	1
0	30	14	3
P+	48	42	6
P–	21	5	0
M	20	16	2
MN	34	19	3
N	15	12	1
K+	6	4	1
K–	53	44	10
CD (Rh_1 Rh_1)	11	16	1
CcD (Rh_1 rh)	27	16	2
CcDE (Rh_1 Rh_2)	11	3	1
DE (Rh_2)	12	6	2
D (Rh_0)	2	1	0
cde (rh–)	6	5	0

Table 2

Relation between Gc- and P-groups in 122 children

	Gc 1–1	Gc 2–1	Gc 2–2
P+	43	37	11
P–	17	13	1

Table 3

Relation between Gc- and haptoglobin groups

	Gc 1–1	Gc 2–1	Gc 2–2
Hp 1–1	10	9	1
Hp 2–1	28	12	1
Hp 2–2	21	17	3

Summary

1. A new serum system (Gc) has been studied in relation to certain blood and serum groups.
2. No relation between blood groups and the Gc groups was found except for the P-system which showed a significant association with the Gc-groups in a sample consisting of adult women, but not in their children.
3. The Gc-groups do not seem to be identical with or closely related to the Hp-, Gm-, transferrin- or cholinesterase groups.

Zusammenfassung

1. Ein neues Serumsystem (Gc) und seine Beziehungen zu bestimmten Blut- und Serumgruppen wurden untersucht.

2. Ein Zusammenhang zwischen Blutgruppen und den Gc-Gruppen besteht nicht, mit Ausnahme des P-Systems. Hier zeigte sich bei einer Gruppe erwachsener Frauen eine signifikante Beziehung zu den Gc-Gruppen. Diese bestand jedoch nicht bei ihren Kindern.

3. Die Gc-Gruppen scheinen mit den Hp-, Gm-, Transferrin- oder Cholinesterase-Gruppen weder identisch noch eng verwandt zu sein.

Résumé

1° Un nouveau groupe sanguin (Gc) a été étudié en ce qui concerne ses rapports avec certains groupes de sang et de sérum.

2° On n'a pas trouvé de relation entre les groupes sanguins et les groupes Gc exception faite pour le système P qui montre une association significative avec les groupes Gc chez un groupe de femmes adultes, mais pas chez leurs enfants.

3° Les groupes Gc ne semblent pas être identiques ou apparentés avec les groupes Hp, Gm, transferrine ou cholinestérase.

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SEX-LINKED DEAFNESS OF A POSSIBLY NEW TYPE

By JAN MOHR and KRISTOFFER MAGERÖY

Introduction

The relative occurrence of the various genetic causations of deafness has been assessed rather differently by different authors. The prevailing view until recently appears to be that teh inheritance is recessive in the great majority of cases, a dominant mode of inheritance occurring seldom.

Chung, Robison and Morton (1959) on the other hand, were led to assume a rather common occurrence of dominant inheritance. Analyzing by refined statistical methods the most comprehensive recent study of deaf mutism, namely that carried out by *Stevenson and Cheeseman* (1956) on the population of Northern Ireland, they concluded that the congenital deaf mute population appeared to consist of the following three types:

(1) Autosomal recessives, complete penetrance, 68% of cases, at least several loci.

(2) Autosomal dominants, high but incomplete penetrance, 22% of all cases, at least two loci.

(3) Sporadic cases, due to unrecognized infection of more complex genetic mechanisms.

A sex-linked mode of inheritance, which seems from earlier reports (see below) to occur, was not demonstrated by this data, though it is suggested by some of the shorter pedigrees. The general excess of males among deaf

mutes, which has been observed by various workers (*Stevenson and Cheeseman*, 1956; *Furusho*, 1957; *Lindenov*, 1945), may also be due to sex-linked causes, and on this assumption *Chung, Robison and Morton* (1959) tentatively estimated that 1.3% of the deaf mutes might be of this kind.

The present paper will perhaps serve in one respect to amplify the picture of genetic deafness, in that it shows that not only the two autosomal categories mentioned above may be genetically heterogeneous, but also the sex-linked group: A kindred is presented that shows a kind of sex-linked deafness which has apparently not been described before, and which might appropriately be termed *progressive sex-linked deafness*.

Earlier data on sex-linked deafness

The occurrence of sex-linked deafness was indicated by the reports of *Sataloff et al.* (1955) and *Parker* (1958). The first of these concerns a kindred comprising 7 male patients, distributed over 4 generations. The hearing loss was severe in all the patients, audiograms showing in all the 6 patients for whom it was obtained, a hearing loss of more than 60 decibels in the whole frequency range, and more than 70 decibels in the middle, major part of the range. One of the subjects was able to speak fairly intelligibly. This patient was a 16-year-old boy attending a school for the deaf. His audiogram showed the defect to be relatively mild, although with a hearing loss of more than 70 decibels in the frequency range 500–4000. He was using a hearing aid with fair results. The rest of the 7 patients in the kindred were deaf mute. With regard to the development of the defect, there was, judging by the report, no indication of the deafness not having been present from birth, or of any progressiveness. None of the patients had any offspring. Only four of the patients were adult at the time of the study. All these were over 36 years.

The second report also relates to a single kindred, in this case comprising 14 affected members, distributed over 3 generations. Here the deafness was uniformly severe, the audiograms showing hearing loss in all patients to be more than 70 decibels for all frequencies. The speach development was rudimentary in all patients. As in the former kindred, there was no evidence that the defect was not present at birth, or that it had been progressive. With regard to propagation, one of the patients in this kindred was married, and had a son with normal hearing.

No indication was found that different genes were concerned; indeed *Parker* suggested that the defect in these two kindreds might have a common ancestry.

The present kindred

The present kindred comprises 11 male patients distributed over 4 generations, as shown in fig. 1. The individual V 13 may be considered the propositus. His mother, who had become pregnant again, was afraid that her next child might also become affected. At her request, abortion was provoked (V 14).

It may be of some interest to follow the defective gene in its geographical localities through the generations. The defect was traced back four generations from the propositus to a female (I 1), who on the hypothesis of sex-linkage must have been a heterozygote. Her home was in Nordvik, a little fishing village on an island in North Norway, about midway between Narvik and Trondheim. This supposed carrier passed on the gene to two of her sons (II 1 and 2), and to her daughter (II 3). This carrier moved from Nordvik to Vannved, a fishing village on an island about 10 kilometres from Nordvik. She transmitted the gene to two (III 1 and 6) of her four sons, and to at least two (III 11 and 12) of her five daughters. Of these two carrier females, the first passed on the gene to her single male child (IV 3), while the other, who moved to Skibbåtsvær, a little island out in the ocean about 25 kilometres from Vannved, transmitted it to 3 (IV 11, 15 and 19) of her four sons, and to at least two (V 8 and 13) of her seven daughters. Of the two certain carrier daughters (IV 8 and 13), the first, who moved to Heröyholmen, an island about 20 kilometres from Nordvik, passed on the gene to both her sons (V 7 and 8), while the other carrier (IV 13) transmitted it to her single son (V 13), who may be considered the propositus.

An attempt was made to trace the kindred farther back and down again through collaterals, but no further cases were discovered by this investigation.

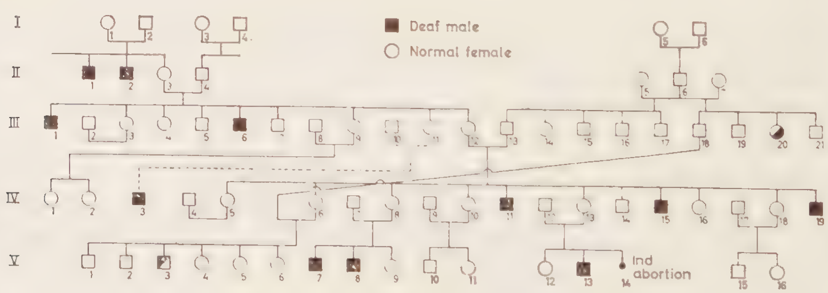

Figure 1

Kindred with progressive sex-linked deafness. Individuals V 3 and III 20 are cases of mental deficiency.

The patients

V 13, b. 19.5.1949, male. Propositus. According to his mother, he learned at first to speak like other children, although he talked somewhat loudly. He enjoyed singing very much. From about 3 years of age there was a steady decline of hearing, with a decline also in ability to speak. – The patient is the younger of two children. Birth occurred spontaneously at term. Psychomotoric development seems to have been normal during the first 3 years of life. He played in a natural way with other children. From about 2 years of age, when his parents moved to Oslo, he was largely in the care of the father's parents, who live on a lonely island off the coast of Nordland. There were several small children, so he had full opportunity to be together with children of his own age. Gradually he developed a difficult attitude, agressive and occasionally sadistic, which made him hard to handle. At 6 years of age he was observed by the district medical officer, *Heröy*, who in his report states that besides being hard of hearing the boy was very much afraid. It had been found impossible to bring him to the doctor, since he went completely wild, although he had never been subjected to any painful medical treatment. In his home it was also impossible for the doctor to establish contact with the patient. In the doctor's report he is described as having an alert, frightened expression, which with other aspects of his behaviour indicated that the case was not one of mental defect. He was admitted to the Department of Child Psychiatry, Rikshospitalet, 1956, where the hearing was found to be so much reduced that he did not react when spoken to from behind, although he appeared to do so when a cow bell was rung behind him. He was able to talk, but it was often difficult to understand what he said. The vocabulary was small, the sentences being simple, and the use of words often faulty.

General examination, Rikshospitalet 1956: Somewhat small of stature and dysplastic, slightly cyanotic cheeks and extremities. Conspiciously dry and thin hair.

Dermatological Department: Mild seborrhoic exzema.

Ophthalmological Department: Divergent strabismus, mild myopic astigmatism.

Ear–Nose–Throat Department: Neurogenic deafness of serious degree, negative findings by X-ray examination of temporal bone and cranium. Thickened mucous membrane in right maxillar sinus.

Encephalography: Central defect, possibly enlargement of 3rd ventricle? (Incomplete examination.)

EEG: Nothing definitely pathological, but background activity somewhat irregular and slower than usual.

Neurological examination: Nothing pathological apart from that already mentioned.

Urine: Normal findings. Haemoglobine 97%, sedimentation rate 10 mm/hr. Meinicke's reaction in blood, negative.

Spinal puncture: Normal findings. Wassermann's reaction in spinal fluid, negative. Mastix reaction, normal.

Psychological examination: Anxiety reaction with compulsive components, generally infantile. Intelligence probably normal.

V 8, b. 23.3.1948, male. According to his mother he learned to speak like other children until 3 or 4 years of age. At that time she recognized a defect of hearing, and from then on the ability to speak regressed. The affection was, however, sufficiently mild to enable him to attend regular State school for a year. Speach was then defective, and he was transferred to the Trondheim State School for the Deaf 1957. When applying for admission, his father stated (1956) that the patient had been defective of hearing since early infancy.

Concerning the development of the defect it is of interest to note that in his mother's opinion he was at the age of 3 years better at speaking than his older brother, who was then 8 years old, and only relatively mildly affected (see below), but as the defect developed, he became more seriously affected than his brother.

V 7, b. 3.12.1943, male. Brother of the preceding. Defect of hearing was noticed by the mother at 3 or 4 years of age, as in the case of the brother. The defect took, however, a milder development in this case, and although he is clearly weak of hearing, he manages fairly well. He has some difficulty in speaking, but can express himself clearly, and he reads in a perfectly comprehensible way. Attends normal State school. According to his mother (1957) it has not been found necessary for him to attend a special school for the deaf.

V 3, b. 26.1.1945, male. Doubtful case. According to his mother he hears, speaks, can read and do elementary sums, but is somewhat backward mentally. Has attended normal State school. He has not been to a physician, except for routine medical examination at school.

IV 19, b. 23.5.1938, male. According to his father he learned to speak like other children at first. Later deafness set in and is now of a high degree. Admitted to Trondheim State School for the Deaf 1947. Later transferred to other deaf schools. Audiogramm 1951: Hearing loss of 80 decibels or more in the range 500–4000 cycles. Report at end of stay at Borre School for the Deaf 1955: "Profits fairly well from theoretical teaching. Will probably be able in part to take care of himself and not need support or special care by the State. Will return home after finishing school."

According to the district physician (1957), he cannot now talk comprehensibly; can only produce some simple sounds which the parents alone are able to interpret.

IV 15, b. 18.8.1930, male. As in the case of the preceding patient, his brother, the father states that he learned to speak like other children at first. He seems also to have enjoyed singing. Started school very late because he was in care at home during the war. Admitted 1952 to Trondheim State School for the Deaf. By this School he was characterized as deaf, of normal intelligence, his hearing being too feeble to be of any help for learning. According to the district physician (1957) he cannot now talk comprehensibly; can only produce some simple sounds that the parents alone are able to interpret.

IV 11, b. 19.7.1924, male. Defective hearing according to his sister (IV 13) and father (III 13). Is said not to have attended school because of mental deficiency.

IV 3, b. ca. 1941, male. In care of family outside his kindred. Has attended Trondheim State School for the Deaf.

III 1, b. 23.7.1897, male. Deaf according to IV 13, The Population register, Heröy, and Trondheim State School for the Deaf. Dead.

III 6, brother of III 1. Deaf according to IV 13, The Population Register, Heröy, and Trondheim State School for the Deaf. Dead.

II 1, b. 1893, male. Deaf according to census of the population 1900 (and IV 13).

II 2, brother of II 1. Deaf according to III 13.

The sibships of generation II as shown on fig. 1, are not complete. In the first sibship

of this generation there are 3 more sons and 3 more daughters than shown, whereof one daughter died in infancy, all apparently unaffected.

Discussion

(a) Mode of inheritance

From the pedigree shown in Fig. 1, it emerges that the defect occurs in 4 consecutive generations, affecting in all the 6 sibships concerned, only males. These sibships comprise a total of 35 individuals, whereof 17 are males and 18 females, 11 of the males being affected. In all the 6 families concerned, both parents are unaffected, and the connection with the affected kindred is through the mother. The affected individuals have in no case reproduced.

Among the various genetic possibilities, only the following four simple ones shall be considered: (1) autosomal recessive, (2) autosomal dominant with incomplete manifestation, (3) autosomal dominant with complete sex limitation to males, (4) sex linked recessive.

The first possibility appears practically ruled out already by the general appearance of the pedigree. In the case of a rare recessive gene, the defect would only in rare instances appear in four consecutive generations of a kindred; the fathers in all the 6 affected families of the pedigree would on this hypothesis have to be carriers, which would be extremely improbable for persons not related to an affected individual; no such relationship was found for any of the 6 fathers.

The second possibility is not so far fetched as the first, though still very unlikely. The distribution within the 6 sibships deviates significantly from that expected on this hypothesis, in males only being affected, also, the transmission through females only, is at variance with the hypothesis, though this fact considered alone could easily be due to a chance variation.

The two last possibilities, sex limitation (3) and sex linkage (4), are both compatible with the data; not only do the distributions within the 6 sibships agree well with the expected distribution ($\chi^2_{(2)} = 1.5$, $0.30 < P < 0.50$) but also the transmission through females only is in accordance with expectation on both hypotheses, given that the affected individuals, as has been the case in the present kindred, do not reproduce.

The difference between possibilities (3) and (4) would only be conspicuous in the case of propagation of affected individuals, the hypothesis of sex linkage being incompatible with transmission directly from father to son, while on the hypothesis of sex limitation the affected fathers would be expected to transmit the defective gene to half their sons.

Another possibility of distinguishing between these two hypothesis is a study of linkage. A demonstration of linkage of the defect with a sex linked trait such as colour blindness would decide in favour of the hypothesis of sex linkage. In view of the rarity of the condition, this admittedly appears at present more a theoretical than a practical possibility.

Strictly speaking, it is impossible to say on the basis of the present material that the mode of inheritance is sex linkage: but from the relatively common occurrence of this mechanism, it seems to be decidedly the most probable one, and this hypothesis may be assumed to be correct, in default of contradictory evidence.

(b) Probable distinctness of the present defect from earlier described types of deafness.

A striking feature of the present kindred is the apparent progressiveness of the deafness. There is suggestion of this in all the five patients for whom detailed information is available, namely V 13, V 8, V 7, IV 19, and IV 15.

Unfortunately no objective determinations of deafness and its corrolary, defect of speech, has been carried out during the first years of life. The hypothesis of progressiveness rests therefore almost solely on information from relatives.

The information respecting ability to speak is presumably more reliable than concerning deafness, and has therefore particular interest. With regard to V 13, the propositus, it seems clear from the history that hearing must earlier have been sufficiently good to assist in speech development, whereas at the time of medical examination it was too feeble for this. In this instance the case for progressiveness appears good.

With respect to V 8, the information from the father to the effect that hearing was defective from early infancy may appear to be at variance with the mother's information of the patient having at first learned to speak like other children. It seems safe, however, to assume that he talked better at some earlier period than later, and that, according to the mother's statement, he talked better at some period than his older, mildly affected and apparently fairly stationary brother (see below). Later (1957) he was, according to the district physician, able to produce only a few sounds. Here too the case for progressiveness seems fair.

With regard to the more mildly affected brother, V 7, the question of progressiveness is less clear, although also in this case the mother states that speech development at first proceeded normally and then regressed. As stated above (page 58), his afflication is mild, so the possible regression must have been modest.

The affected maternal uncles of these three patients, IV 19 and IV 15, seem to be clearly progressive cases, although the father's statement that they at first learned to speak like other children, should perhaps be taken with caution. It may apparently be safely assumed that they were at first not mute. Today they can only produce simple sounds (page 58).

As far as hearing ability can be assessed by speaking ability in cases like the one under discussion, the suggestion is strong that progressiveness of development is a characteristic feature of the present defect. Whether an interval of fully normal hearing may proceed the appearance of deafness, or if some degree of hearing impairment is in all cases present already from birth, cannot be decided on the basis of the available data. Nor is it clear whether cases occur in which deafness is already from birth too serious to be of any guidance in speech development.

The earlier described cases of sex-linked deafness (*Sataloff et al.*, 1955, and *Parker*, 1958) do not, according to the reports, show any progressiveness. In view of the rather dramatic impression such a development is apt to produce, it seems unlikely that it could have been overlooked in the earlier described cases. It seems more likely that the present is a peculiar type of sex-linked deafness, different from those earlier described.

As to location in the chromosome, it is of course impossible to say whether the locus concerned is the same in all the three hitherto described kindreds of sex-linked deafness. With such rare defects the only genetic method by which it is possible to approach the question whether more than one locus is involved, seems to be a study of linkage. This is clearly a rather theoretical proposition in the present case, although in the long run results might be attained.

In view of the probable sex-linkage and the apparent progressiveness of the defect, it might appropriately be termed *progressive sex-linked deafness.*

Summary

Hereditary deafness in a kindred comprising affected individuals in four generations, in all 11 male patients, is described, the familial distribution suggesting sex-linked inheritance. The condition seems to be different from the cases of sex-linked deafness described earlier, in showing progressive development with gradual loss of speech after an interval in which hearing is generally not sufficiently impaired to prevent speech development. It is suggested that the designation *progressive sex-linked deafness* might be appropriate.

Zusammenfassung

Erbliche Taubheit wird bei 11 männlichen Patienten einer durch vier Generationen verfolgten Sippe beschrieben. Die familiäre Verteilung läßt auf geschlechtsgebundenen Erbgang schließen. Dieser Typ von erblicher Taubheit unterscheidet sich offenbar von allen bisher beschriebenen Fällen. Er zeigt eine progressive Entwicklung mit langsamem Sprachverlust. Dieser Entwicklung geht eine Zwischenstufe voraus, in der das Hörvermögen im allgemeinen nicht so beeinträchtigt ist, daß die Sprachentwicklung gehindert wird. Als geeignete Bezeichnung wird «progressive geschlechtsgebundene Taubheit» vorgeschlagen.

Résumé

On décrit une surdité héréditaire dans une famille comprenant des individus atteints dans quatre générations. Le fait que les onze malades sont du sexe masculin parle en faveur d'une transmission liée au sexe. L'affection semble être différente de la surdité liée au sexe, décrite auparavant, puisqu'on constate une évolution progressive avec perte graduelle du langage, après un intervalle pendant lequel l'ouïe n'est en général pas assez compromise pour empêcher le développement du langage. On propose le nom de surdité progressive liée au sexe.

Acknowledgements

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THE SIMULATION OF MENDELISM

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Mendelism, in its original sense, refers to the segregation of characters in such a manner that their inheritance may be explained in terms of their being the consequence of a single factor, or of a pair of single factors, and these concepts have been successfully applied to a large number of rare diseases in man.

Familial concentration is a feature common to all diseases in man; in some, as in silicosis, malnutrition and schizophrenia, the familial concentration is so striking that it is necessary to postulate some innate or acquired peculiarity common to such families. An innate peculiarity may be variously conditioned; in addition to single factor inheritance a large number of characteristics are now known to be dependent upon the additive effects of a multiplicity of genes, and such characteristics may appear discontinous or, in Grüneberg's terminology, quasi-continuous.

The threshold or line or dichotomy may be due to developmental variations, as in the case of the foramen ovale of the mouse acetabulum, in which it appears that the genetic determinants related to the formation of this hole, if present at less than a certain intensity, are inadequate to lead to its development (*Grüneberg*, 1951).

In man such developmental abnormalities as cleft palate, hare lip, anencephaly, spina bifida and most heart defects, which are probably related to the unpunctual fusion of the margins of various grooves and holes, may be conditioned by continuous variations, innate and acquired, in developmental punctuality.

In other conditions the threshold is biochemical, the response to some substance showing some sudden discontinuity, as in the various hormonal

switch mechanisms, or in the crystallization, incorporation or overflow which develops at above a certain level, as in gouty deposits, atheroma, or glycosuria. In other cases the discontinuity may be mechanical, as in the bursting of an artery in apoplexy or sub-arachnoid haemorrhage being predisposed to by high internal pressures and thin or diseased walls.

The discontinuity is not necessarily explicit in the data but may be entirely imposed by the observer for semantic economy, as in such words as thin, neurotic and hypertensive, or for administrative convenience, as in recording the eleven-plus examination or in the specification of prematurity.

In many cases of disease it may be self-perseverating, so that, once a certain level of abnormality is present, further damage occurs of such a nature that it excites the mechanism causing damage. Malignant hypertension, in which a vicious circle becomes established through pressure damage to the arteries increasing their resistance, is a simple example. Others include the social isolation induced by eccentricity, the intellectual deprivation of the institutionalized defective, and the physical inactivity of the very fat. In diabetes it is usually maintained that adequate control reduces the rate of increase of insulin requirements, and this suggests that a vicious circle may be established at an earlier stage in the disease. In focal epilepsy there is extensive clinical evidence suggesting that the influence of the focus increases with each fit. All such vicious circles will have the effect of causing a break-away at one end of any continuous distribution to which they are related, and in such cases an overt bimodality may overlie a basic continuity.

The concept of quasi-continuous variation in relation to human disease was clearly defined in the Hippocratic doctrine of diathesis, a diathesis being an inherited continuum extremes of which are pecularly predisposed to the development of various diseases. The concept was explicitly related to congenital malformations by Darwin, who regarded these as the likely price of an extreme variability, while more recently *Lerner* (1953) has advanced a similar hypothesis with special reference to the increase in phenotypic variability resulting from an increased homozygosity.

When the variates underlying these discontinuities show familial correlations, the discontinuities will show familial aggregations, and, when the correlations are high and the disorder common, these familial aggregations may be so high that they simulate the pattern of inheritance expected in single factor inheritance. If the qualification of necessity is removed by the concept of penetrance, the hypotheses may be indistinguishable on even extensive observational data.

As nearly all disorders develop from a stage of apparent normality, there are times when the manifestation of disease is only present in a proportion of disposed cases, and, in such cases, this proportion is termed the penetrance. In other conditions the variability of other developmental influences is such that manifestation may occasionally not occur as in the common forms of polydactyly, or may only occur under extreme conditions, as in haemophilia, or osteogenesis imperfecta, which may only become manifest under considerable trauma. In other conditions, as Huntington's chorea or polycystic kidneys, death from other causes commonly precedes the usual age of manifestation. In such relatively rare conditions, whose incidence does not exceed 1 per thousand or so, and is usually less than 1 in 10,000, and in which our observational powers do not allow the genotype to be specified by the phenotype, the concept of penetrance appears not merely valuable but inescapable.

This concept is, however, often used in relation to common disorders when it is a refuge for an ignorance which it is the business of the investigator to disperse rather than to concentrate. Like the epicycle of Ptolemy it revolves round nothing and, like the epicycle, should only be invoked if alternative explanations, even if of greater analytic complexity, prove less adequate. Further, the assumption of the constancy of penetrance in different individuals assumes an independence of both the inherited constitution and the environment, neither of which is likely. If the penetrance is assumed to vary in relation to either the genetic background, or the environment, or both, then it is difficult to see how this can be manifest other than in an effectively quasi-continuous manner. In this case the difference between single gene concepts with penetrance and quasi-continuous variation is the difference between a single gene combined with multifactorial inheritance and multifactorial inheritance alone. The former hypothesis is more complex and shades into the latter as the single gene becomes of diminishing effectiveness or "lower penetrance".

If we consider the simple cases of multifactorial inheritance, and of an abrupt threshold such that a proportion p of the population lies beyond it, then the intensity of familial aggregation shows a simple approximate relationship to p. In practice the threshold is not abrupt, which has the effect of reducing the genotype intraclass correlations. On the other hand the environmental features common to families, and, in the case of siblings, the common uterus and similar post-natal handling, will have the effect of increasing the phenotypic correlations. In the case of first degree relatives the correlations of the genotypes will be approximately $\frac{1}{2}$ and, more generally, in the n the degree relations $(\frac{1}{2})^n$.

In the case above we may ask; firstly, what is the incidence in the *n* th degree relatives of a propositus? Secondly, to what extent does this incidence exceed the population incidence? The former question is of primary interest to the geneticist who examines formal data; the latter to the clinician who tends to base his opinion on the familial tendencies of diseases on the extent of the excess risk of relatives. *Penrose* (1953) has discussed this increase in liability, which he terms *k*, in relation to dominant, intermediate and recessive inheritance in common diseases.

If we consider any relative of a propositus, and the relationship is such that the intraclass correlation is r, then we may specify the above question with reference to the quadrants of the bivariate normal surface in figure 1.

Figure 1

Diagram showing the incidence of affected first degree relatives of propositi in quasi-continuous inheritance. The ellipse represents an arbitrary contour on the bivariate normal surface of correlation r = 0.5. The lines represent the dichotomizing planes defining the level of discontinuity or the threshold of specification: as these are equal in the propositus and their relatives the diagram is symmetrical about the main diagonal.

The bivariate normal surface defines the expected distribution of a mass of points, each representing the relevant parameters for each pair of relatives. The dichotomies which divide the continuum into two discontinuous segments, and the surface into four quadrants, represent the thresholds which will be equal. If the numbers *a, b, c, d* represent proportions, and a + b + c + d = 1, then if *p* is the population incidence of the disorder

$$p = b + d$$

the incidence in specified relatives of the propositus is

$$\frac{b}{b + d}$$

and the ratio of this incidence to the incidence in the general population is

$$\frac{b}{(b + d)^2}$$

The proportions a, b, c, d exhibit the approximate relationship

$$\ln \frac{bc}{ad} \simeq \frac{8}{\pi} z \qquad \text{where } z = \tanh^{-1} r$$

and this is largely invariant to the levels of dichotomy (*Edwards*, 1957). In the symmetric case when the planes of dichotomy are equidistant from the mean the approximate relationship

$$b \simeq (b + d)^{t}$$

where t is a constant is also largely invariant to the levels of dichotomy (*Sandon*, 1957). It may be shown by substitution that the satisfaction of these approximate identities implies the approximation

$$t \simeq 1 + \ln(1 + e^{-8z/\pi}) / \ln 2$$

which varies between 2 and 1 as r varies between 0 and 1. The approximation becomes progressively less exact as the distance of the dichotomies from the centre increases. When r = 0.5, the value $t \simeq 1\frac{1}{2}$ is simple and adequate to a first approximation, and, in this case, the incidence in first degree relatives

$$= (b + d)^{(t - 1)} \simeq p^{1/2}$$

and the ratio of this incidence to the population incidence

$$= (b + d)^{(t - 2)} \simeq p^{-1/2}$$

Figure 2 shows this approximation, and compares it to exact values calculated from the tetrachoric tables of Karl Pearson. It is seen that when p is less than about 16% the incidence in first degree relatives exceeds $p^{1/2}$.

It is interesting to note that in the range of incidence between 0.1% and 1.0%, within which lie epilepsy, schizophrenia, diabetes, spina bifida, anencephaly, pyloric stenosis and mental deficiency of unknown cause, the incidence in first degree relations expected on a multifactorial hypothesis is very similar to that found. In the common conditions of schizophrenia and diabetes the incidence in first degree relatives is such that hypotheses of recessive inheritance have been authoritatively entertained. In these two conditions the frequent association with failure to marry and procreate respectively, and the fact that families often contain more children than parents, have given further irrelevant support to such hypotheses.

Some additional information relevant to these hypotheses may be obtained from the incidence in cousins, aunts and uncles, or other more distant relatives. Such additional information is however of very little help

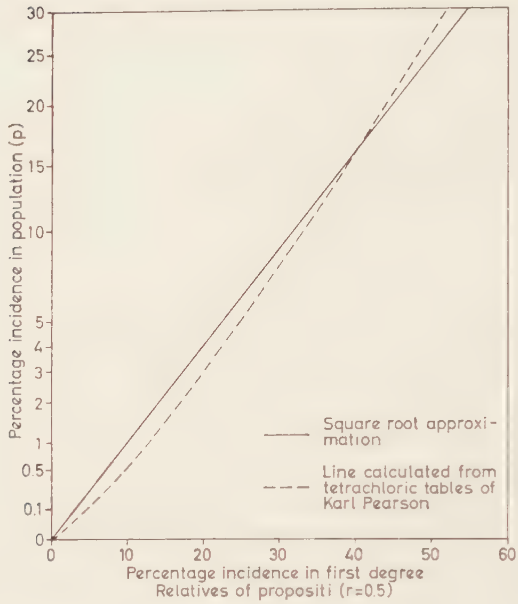

Figure 2

as the operational similarity of the two hypotheses persists. This is hardly surprising as in both hypotheses the more distant the relationship the lower the incidence. We may express the incidence and relative incidence in various relatives on the three hypotheses of dominant, recessive and multifactorial inheritance (tables 1 and 2).

There are, however, two observable consequences of multifactorial inheritance which differ from single factor inheritance. Firstly, in the former the risk to the unborn increases with the number of relatives affected. If, for example, two sibs are affected in one two-child family, and one in

Table 1

Incidence in relatives of propositi

	Dominant	Recessive	Multifactorial
Sibs	$^1/_2$	$^1/_4$	$\simeq p^{1/2}$
Parent or child	$^1/_2$	$p^{1/2}$	$\simeq p^{1/2}$
First cousin	$^1/_8$	$^1/_4 p^{1/2}$	$\simeq p^{4/5}$

Table 2

Relative incidence in relatives of propositi

	Dominant	Recessive	Multifactorial
Sibs	$\frac{1}{2}p^{-1}$	$\frac{1}{4}p^{-1}$	$\simeq p^{-\frac{1}{2}}$
Parent or child	$\frac{1}{2}p^{-1}$	$p^{-\frac{1}{2}}$	$\simeq p^{-\frac{1}{2}}$
First cousin	$\frac{1}{8}p^{-1}$	$\frac{1}{4}p^{-\frac{1}{2}}$	$\simeq p^{-\frac{1}{5}}$

another, the risks to any further sib will be higher in the former family on a multifactorial hypothesis but equal on a single factor hypothesis. The expected extent of this excess risk must await tabulation of the partitions of the symmetrically dichotomized trivariate normal hypersurface. Secondly, when the arbitrarily dichotomized variate is measurable, as in height, gout or feeble mindedness, there should, on the multifactorial hypothesis, be no bimodality in the scores, unless some self-perpetuating mechanism can reasonably be postulated as in hypertension or glaucoma; further, if dominant inheritance is simulated, the hypothetical non-carrier parent should tend to have above-average scores.

Attempts to discover so-called carriers by imposing special stresses, as in giving cortisone to the relatives of diabetics, or flashing lights at the children of epileptics, cannot necessarily provide any distinction between single gene and multiple gene hypotheses, although they may appear to confirm the former as it will often be possible to find a stress which will lead to the desired segregation ratio. To take an analogy, if we arbitrarily defined tallness in women as being more than 5′ 8″ tall, it would be possible, by trying out various types of high-heeled shoes, to find brands which would provide a segregation ratio appropriate to the required genetical hypothesis, and to define women on whom tallness was thus imposed as exhibiting latent tallness.

Although these two types of inheritance may lead to similar patterns of familial aggregation, their distinction is far from trivial in importance. If single genes of impaired penetrance are involved then an increase in the mutation rate will lead to an increase in incidence of the disorders to which they predispose. If, on the other hand, the manifestation is the result of multifactorial inheritance, no prediction can be made of the influence of an increased mutation rate without assuming values for several unknown parameters.

Summary

The operational distinction between quasi-continuous variation and the effects of major genes of low penetrance is discussed.

It is shown that, in quasi-continuous variation, a trait with an incidence p would be expected to have an incidence of the order of $\sqrt{p}$ in the first degree relatives of propositi.

Zusammenfassung

Die methodische Unterscheidung zwischen quasi-kontinuierlicher Variation und den Wirkungen von Hauptgenen mit niedriger Penetranz wird diskutiert.

Es wird gezeigt, daß bei quasi-kontinuierlicher Variation ein Merkmal mit der Wahrscheinlichkeit p bei den Verwandten 1. Grades des Probanden eher eine Wahrscheinlichkeit $\sqrt{p}$ haben muß.

Résumé

L'auteur discute la différence entre les variations presque continues et les effets des gènes principaux ayant une faible pénétrance. Il montre que lorsque dans une variation presque continue la fréquence d'un caractère est p, la fréquence probable de ce caractère chez les parents du 1er degré du proband est $\sqrt{p}$.

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FREQUENCIES OF CONSANGUINEOUS MARRIAGES IN NORTHEAST OF SÃO PAULO, BRAZIL[1]

By P. H. SALDANHA

Introduction

The proportion of homozygotes for rare recessive genes is likely to be higher among children from consanguineous marriages than from unrelated individuals. This has been confirmed by studying the frequencies of first cousin marriages among the parents of affected individuals (for formulae, see *Dahlberg*, 1947). For the better known recessive genes this fraction has been estimated to range from 10 up to 80 per cent (*Neel and Schull*, 1954, table 7–5) and the variation is due to different gene and cousin marriage frequencies of the populations investigated or, in other words, due to the occurrence of isolate effects.

The actual increase of the homozygote frequency, caused by inbreeding is negligible in Panmixia, even among populations of very small size. In the case of relative increase of affected people with rare recessives compared to a population of infinite size ($\alpha = 0$), the homozygote frequency should be larger when the gene frequency decreases, but, in Panmixia, an appreci-

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[1] This work had financial support from the Rockefeller Foundation.

able rate of consanguineous marriages is to be expected only in isolates of very small size. In this situation, it should not be possible to find very low gene frequencies.

However, the study of rates of consanguineous matings gives information about the population structure since, in Panmixia, these rates reflect the isolate size (*Dahlberg*, 1929). In comparative population studies, data on frequencies of consanguineous marriages are important in order to state genetic differences. Among the genetic problems for which the knowledge of rates of consanguineous marriages is relevant, is the evaluation of the following parameters: isolate size and effects, frequencies of rare recessive genes, of mutation rates and load of detrimental recessive genes in populations, effects of radiation on the frequency of recessive genes, etc. The available data on frequencies of consanguineous marriages in different countries have shown that they are very heterogeneous (Table 1). This is expected to be caused by different geographical and social patterns of the populations.

The variation of consanguinity rates in time has been shown by using the Catholic parish registers of marriages. A general decline of the mean coefficient of inbreeding (α)[2] has been detected mainly in the communities of Europe and America, and it is interpreted as the result of intermixture of previously isolated populations (breakdown of isolates, *Dahlberg*, 1938; 1947). An important consequence of the miscegenation is that the balance between mutation and gene elimination has been disturbed. *Haldane* (1939) has shown that a new equilibrium is to be expected after hundreds of generations. This means that the western populations are not in equilibrium for completely recessive genes, since the breakdown of isolates is a relatively recent event.

The decrease of inbreeding rates has been noticed in the following countries: Bavaria and Prussia (*Dahlberg*, 1938), Germany (*Müller*, 1953; *Verschuer*, 1954), France (*Sutter and Tabah*, 1951), USA (*Herdorn and Kerley*, 1952; *Woolf and al.*, 1956), Sweden (*Romanus*, 1953; *Böök and Måwe*, 1955; *Böök*, 1956; *Larson*, 1956; *Fraccaro*, 1958), Brazil (*Freire-Maia*, 1952; 1957b), India (*Sanghvi et al.*, 1956), Italy (*Cavalli-Sforza*, 1956) and Belgium (*Deraemaeker*, 1958). However, practically no study has been carried on to look for regional differences within areas containing zones with different geographical and social conditions.

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[2] α means the relative increase of homozygosis of populations caused by inbreeding. It is a weighed mean of all consanguineous marriages in the populations, according to its particular inbreeding coefficient in relation to the total number of marriages observed (see: *Haldane and Moshinsky*, 1939).

Country	Period	No. of marriages examined	Marriages between uncles and nieces or between aunts and nephews (%)	First cousin marriages (%)	Other types of cousin marriages (%)	Mean coefficient of inbreeding ($\alpha \times 10^5$)	References
Europe							
Austria	1929–1930	31,823	–	0.53	0.99	–	Orel, 1932
Belgium (Antwerp)	1926–1950	67,920	0.05	0.36	0.47	37	Deraemaeker 1958
Denmark	1900–1920	498	–	1.2	–	–	Bartels, 1941
England and Wales (1)	1924–1929	10,236	0.01	0.40	0.15	28	Bell, 1940
France (General)	1926–1945	4,000,000	0.01	0.72	1.04	66	Sutter and Tabah, 1948
Germany (General) (1)	1899–1951	3,740,854	0.06	0.12	–	–	Dahlberg, 1938; Panse and Krings, 1949; Müller, 1953; Verschuer, 1954
Germany (Jews)	1875–1920	117	–	16.2	19.6	–	Reutlinger, 1922
Holland	1936–1953	1,170,530	0.02	0.16	0.18	–	Freire-Maia, 1957a
Italy (1)	1953	340,693	0.08	0.45	–	39	Fraccaro, 1957
Northern Ireland (1)	1952–1954	10,908	–	0.26	0.56	26	Kilpatrick et al., 1955
Portugal (General)	1940–1955	1,008,672	0.04	1.06	1.10	–	Freire-Maia, 1957a
Sweden (General)	≃ 1946–1950	15,802	–	0.41	0.49	30	Ramanus, 1953
Switzerland (1)	1870–1933	538	–	2.78	15.42	–	Brenk, 1931; Ergenter, 1934; Grob, 1934; Ruepp, 1935
Asia							
India (1)	1901–1955	6,597	–	8.57	4.40	638	Sanghvi et al., 1956
Israel (Ashkenazim)	recent	672	–	1.5 (2)	4.5	–	Goldschmidt and Ronen, 1956
Israel (non Ashkenazim)	recent	1,012	–	9.9 (2)	24.0	–	Goldschmidt and Ronen, 1956
Japan (1)	1929–1948	47,800	–	5.46	3.86	416	Kida et al., 1948; Neel et al., 1949; Schull, 1953
America							
Argentina	1954	23,000	0.03	0.72	1.13	53	Freire-Maia, 1957a
Brazil (General)	recent	–	0.04	2.40	2.12	200	Freire-Maia, 1957b
Jamaica	1929	81	–	8.64	35.80	–	Davemport and Steggerda, 1929
Puerto Rico	1954	6,013	0.02	1.46	5.08	132	Freire-Maia, 1957a
United States (1)	1920–1950	24,865	–	0.13	–	–	Herdorn and Kerley, 1952; Woolf et al., 1956
Uruguay	1952	5,370	0.00	0.82	1.98	63	Freire-Maia, 1957a

1. Recalculated in the present work. 2. Includes also marriages between uncles and nieces or between aunts and nephews.

The purpose of the present paper is to report the frequencies of consanguineous marriages in communities distributed in the Northeastern region of the State of São Paulo, Brazil, and to analyse the population structure of these communities.

The area investigated

The area studied is located between the two main cities of Brazil, Rio de Janeiro and São Paulo. These cities are connected by an important highway, which crosses the valley, Vale do Paraiba, where lie the most populated communities of the region. Bounding the valley, on the inner side, are the Serra da Mantiqueira Mountains and, on the outer side, are the Serra do Mar Mountains. The communities investigated are, there-

Fig. 1. Location of the areas belonging to the Diocese of Taubaté and the Diocese of Piracicaba.

fore, classified as belonging to Vale do Paraiba, Serra da Mantiqueira or Serra do Mar (Figure 1). The demographical, geographical and social patterns of these communities are very different. As an important characteristic, those communities located on the Serra do Mar and on the Serra da Mantiqueira are appreciably isolated and those located on the Vale do Paraiba are subject to strong internal migration movements motivated by the recent improvement in communications and industrialization of the region.

The area belongs to the Diocese of Taubaté. This town was one of the earliest settled in the State of São Paulo and it is still possible to find there descendants of the most ancient families of the State.

A number of communities in the inner part of the State of São Paulo were also investigated (Figure 1). They are located in the Diocese of Piracicaba and since about 1880 have received a very large number of non-Brazilian immigrants, mainly of Italian derivation. Therefore this region furnishes interesting comparative material.

The Data

Data on different types of consanguineous marriages were collected for 32 parishes of the Diocese of Taubaté and for 6 parishes of the Diocese of Piracicaba. About 115.000 Catholic marriage records were examined in the archives of both Dioceses. Since consanguineous marriages are permitted only with dispensation granted by the Bishop, the Catholic marriage register gives direct information concerning marriages between relatives up to third cousin kinship. Frequencies of cousin marriages were analysed for each parish separately and for different periods. The Brazilian population is about 95% Catholic. Therefore parish archives must be reliable for evaluating inbreeding rates. The types of cousin marriages investigated are designated by the following nomenclature: $\frac{1}{2}$ C-marriages between uncles and nieces or between aunt and nephews; 1 C-marriages between first cousins; $1\frac{1}{2}$ C-marriages between first cousins once removed; 2 C-marriages between second cousins; $2\frac{1}{2}$ C-marriages between second cousins once removed; 3 C-marriages between third cousins; CT-total consanguinity; N-total number of marriages. Multiple cousin marriages were considered as respective separate single marriages and counted accordingly. For the estimation of the mean coefficient of inbreeding (α) all types of cousin marriages were considered according to their particular coefficient of inbreeding (*Haldane and Moshinsky*, 1939). Data from parishes of the Diocese of Piracicaba were used only as comparative material.

Table 2. Frequencies of different types of cousin marriages in Northeast of São Paulo (Diocese of Taubaté) in different periods, grouped by region

Period	Type of cousin marriage (%)								
	N	½ C	1 C	1½ C	2 C	2½ C	3 C	CT	α ($\times 10^5$)
				Region of Serra do Mar (9 parishes)					
1800–1806	172	—	—	—	—	—	—	—	—
1830–1836	599	1.61	6.44	2.50	2.32	0.89	1.61	15.38	732
1860–1866	1,891	0.21	3.75	0.37	1.75	0.37	0.48	6.93	305
1890–1896	3,088	0.49	1.85	0.58	1.30	0.19	0.16	4.57	217
1920–1924	2,747	—	1.71	1.20	1.13	—	—	4.04	162
1925–1929	2,903	0.10	1.76	0.72	1.10	—	—	3.68	163
1930–1934	2,590	0.04	1.54	1.04	1.43	—	—	4.05	156
1935–1939	2,953	0.07	1.93	1.05	1.52	—	—	4.57	186
1940–1944	2,064	—	1.84	0.63	1.55	—	—	4.02	160
1945–1949	2,341	0.09	1.75	0.94	2.61	—	—	5.39	190
1950–1954	1,531	0.06	2.48	1.70	3.20	—	—	7.45	266
1955–	260	—	3.08	3.08	1.92	—	—	8.08	319
				Region of Vale do Paraíba (16 parishes)					
1800–1806	457	—	0.22	—	—	—	0.44	0.66	14
1830–1836	696	0.57	3.31	0.57	2.16	0.57	1.29	8.47	340
1860–1866	1,512	0.53	3.44	0.46	1.98	0.53	0.86	7.80	339
1890–1896	4,615	0.46	1.84	0.56	0.85	0.04	0.04	3.79	203
1920–1924	5,425	0.02	1.12	0.29	0.52	—	—	1.95	90
1925–1929	5,635	0.04	0.59	0.28	0.21	0.02	0.04	1.18	56
1930–1934	5,095	—	0.39	0.27	0.22	—	—	0.88	36
1935–1939	6,494	0.03	0.25	0.09	0.18	—	—	0.55	25
1940–1944	5,989	—	0.43	0.05	0.25	—	—	0.73	33
1945–1949	7,072	0.01	0.09	0.04	0.14	—	—	0.28	9
1950–1954	8,279	—	0.22	0.10	0.06	—	—	0.38	18
1955–	2,829	—	0.42	0.11	0.14	—	—	0.67	32
				Region of Serra da Mantiqueira (7 parishes)					
1830–1836	139	—	3.60	—	1.44	0.72	0.72	6.48	324
1860–1866	260	—	1.92	—	0.77	—	—	—	269
1890–1896	912	0.22	3.18	1.32	2.19	0.44	0.55	7.90	357
1920–1924	1,515	—	2.31	0.79	1.12	—	—	4.22	187
1925–1929	1,741	—	1.03	0.69	1.26	—	—	2.99	106
1930–1934	1,464	—	1.50	0.61	0.48	—	—	2.59	121
1935–1939	1,758	—	0.71	0.68	0.80	—	—	3.19	140
1940–1944	1,414	—	1.49	0.78	0.99	—	—	3.26	133
1945–1949	1,556	—	1.48	1.03	1.22	—	—	3.73	144
1950–1954	1,433	—	2.02	0.91	1.26	—	—	4.19	174
1955–	317	—	2.21	0.63	0.32	—	—	3.16	163
				Total (whole Diocese of Taubaté)					
1800–1806	629	—	0.16	—	—	—	0.32	0.48	22
1830–1836	1,394	0.93	4.59	1.29	2.15	0.72	1.36	11.04	488
1860–1866	3,663	0.33	3.49	0.38	1.78	0.41	0.60	6.99	305
1890–1896	8,615	0.44	1.98	0.65	1.15	0.14	0.14	4.50	219
1920–1924	9,687	0.01	1.48	0.63	0.78	—	—	2.90	125
1925–1929	10,279	0.05	0.99	0.48	0.64	0.01	0.02	2.19	93
1930–1934	9,149	0.01	0.90	0.55	0.60	—	—	2.06	84
1935–1939	11,205	0.04	0.92	0.44	0.63	—	—	2.03	85
1940–1944	9,467	—	0.90	0.29	0.64	—	—	1.83	75
1945–1949	10,969	0.03	0.64	0.37	0.82	—	—	1.86	68
1950–1954	11,243	0.01	0.75	0.42	0.64	—	—	1.82	71
1955–	3,406	—	0.79	0.38	0.30	—	—	1.47	66

Table 3. Frequencies of different types of cousin marriages, mean coefficients of inbreeding, and isolate sizes in the Diocese of Taubaté (Northeast of São Paulo), classified by region, and in the Diocese of Piracicaba, for the present and past centuries.

	Consanguinity type (%)								α ($\times 10^5$)	isolate size (n)	average altitude
	N	½ C	1 C	1½C	2 C	2½ C	3 C	CT			
Century XIX											
Diocese of Taubaté (Northeast of São Paulo):											
Serra do Mar (8 p)	6,489	0.46	2.96	0.77	1.59	0.35	0.35	6.49	295	628	–
Serra da Mantiqueira (2 p)	1,311	0.15	2.97	0.92	1.83	0.38	0.46	6.71	267	626	–
Vale do Paraíba (3 p)	7,280	0.45	2.21	0.51	1.15	0.19	0.36	4.88	232	842	–
Total	15,080	0.43	2.60	0.66	1.40	0.28	0.36	5.73	262	715	–
Diocese of Piracicaba: (Capivari)	1,194	0.50	3.68	0.75	1.67	1.26	2.42	10.30	362	505	–
Century XX (between 1920 and 1958)											
Diocese of Taubaté (Northeast of São Paulo):											
Serra do Mar (9 p)	17,389	0.05	1.84	1.04	1.68	–	–	4.61	180	1,011	715
Serra da Mantiqueira (7 p)	11,198	–	1.65	0.78	1.00	–	–	3.43	143	1,127	1,260
Vale do Paraíba (16 p)	46,818	0.01	0.41	0.15	0.21	–	–	0.78	35	4,537	558
Total	75,405	0.02	0.92	0.45	0.66	–	–	2.06	85	2,022	740
Diocese of Piracicaba: (6 parishes)	18,000	0.01	0.40	0.17	0.26	–	–	0.85	32	4,650	548

Table 2 shows the frequencies of different types of cousin marriages, grouped by regions, for different periods. Among the parishes investigated for the present century, nine were located in the Serra do Mar (average altitude: 715 m), seven in the Serra da Mantiqueira (average altitude:

Table 4. Significance of comparisons between rates of cousin marriages obtained for different regions and periods

Region	No. of marriages	No. of non-consanguineous marriages	No. of first cousin marriages	Heterogeneity	No. of non-consanguineous marriages	Total no. of consanguineous marriages	Heterogeneity
XIX Century (Diocese of Taubaté)							
Serra do Mar	6,489	6,297	192	$\chi^2 = 8.23$	6,068	421	$\chi^2 = 19.02$
Serra da Mantiqueira	1,311	1,272	39	2 d.f.	1,223	88	2 d.f.
Vale do Paraíba	7,280	7,119	161	$P = 0.004$	6,925	355	$P \simeq 0.0001$
Total	15,080	14,688	392		14,216	864	
XX Century (Diocese of Taubaté)							
Serra do Mar	17,389	17,069	320	$\chi^2 = 358.65$	16,587	802	$\chi^2 = 148.09$
Serra da Mantiqueira	11,198	11,013	185	2 d.f.	10,814	384	2 d.f.
Vale do Paraíba	46,818	46,626	192	$P < 0.0001$	46,451	367	$P < 0.0001$
Total	75,405	74,708	697		73,852	1,553	
Total (Diocese of Taubaté)							
XIX Century	15,080	14,688	392	$\chi^2 = 296.55$ 1 d.f.	14,216	864	$\chi^2 = 651.01$ 1 d.f.
XX Century	75,405	74,708	697	$P < 0.0001$	73,852	1,553	$P < 0.0001$
Total	90,485	89,396	1,089		88,068	2,417	
Comparison between two Dioceses (XX Century)							
Diocese of Taubaté	18,000	17,928	72	$\chi^2 = 48.93$ 1 d.f.	17,847	153	$\chi^2 = 118.56$ 1 d.f.
Diocese of Piracicaba	75,405	74,708	697	$P < 0.0001$	73,852	1,553	$P < 0.0001$
Total	93,405	92,236	769		91,699	1,706	

1260 m) and sixteen in the Vale do Paraiba (average altitude: 558 m). The remaining six parishes were located on the Central part of the State of São Paulo (average altitude: 540 m).

In order to appreciate the time variation of the frequencies of cousin marriages for the overall area, the data for the present century, classified by region, were compared to the data for the past century, obtained for 13 parishes. The latter includes eight parishes in the Serra do Mar, two parishes in the Serra da Mantiqueira, three parishes in the Vale do Paraíba and one parish in the Diocese of Piracicaba. Table 3 shows the frequencies of different types of cousin marriages obtained for the past and present century, classified by regions.

The rates of cousin marriages for the three groups of communities in the Diocese of Taubaté are statistically different both for the past and the present century (cf. Table 4). A comparison between the rates obtained for the whole Diocese of Taubaté and for the Diocese of Piracicaba shows, for the present century, a similar difference. However, as can be seen from Table 3, a general decrease of the frequencies of marriages between relatives was observed for each region. This decrease is statistically significant and is more striking for the region in the Vale do Paraíba and for the parishes of the Diocese of Piracicaba, which has been subject to a marked non-Brazilian immigration. The present α values for the above regions are appreciably low. In order to evaluate the degree of isolation of the individuals from each region investigated, the respective isolate sizes were esti-

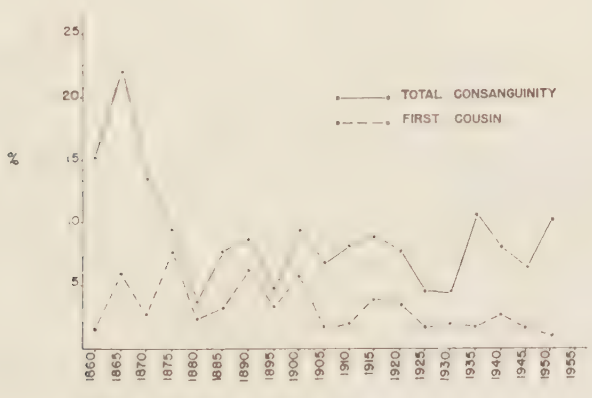

Fig. 2. Frequencies of first cousin marriages and total consanguinity in the Parish of Natividade up to the present time.

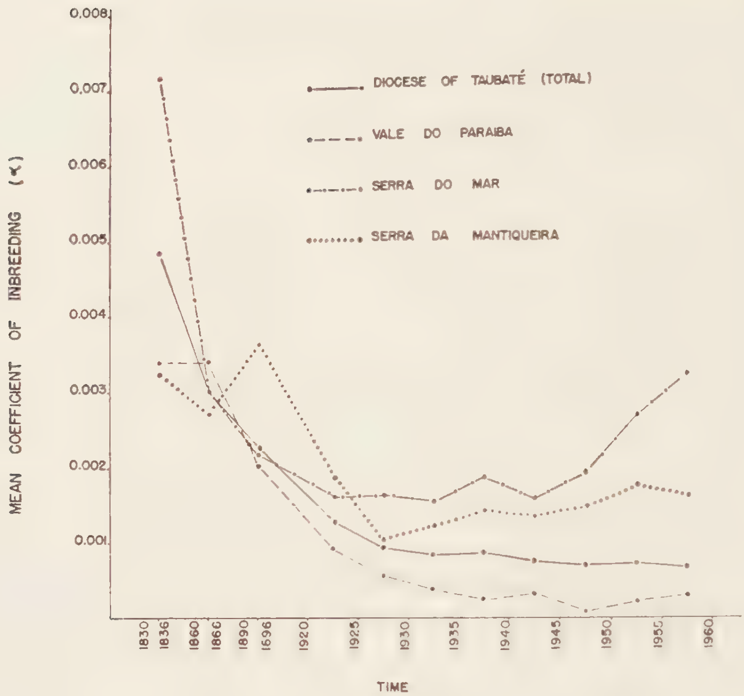

Fig. 3. Time variation of the mean coefficient of inbreeding (α) obtained for the whole and for the three regions of the Diocese of Taubaté.

mated based on *Dahlberg's* formulae and the number of children per terminated family was taken as the present total average for the State of São Paulo (3.59, according to *Mortara*, 1955).

The marriage registers since the foundation of the parish of Natividade were examined up to the present time. This parish is a good representative of the communities located in the Serra do Mar. The variation of the frequencies of first cousin marriages and the total consanguinity obtained for this parish is shown in figure 2. The frequencies of cousin marriages seem to remain stable at a comparatively high level.

Figure 3 shows the variation of the mean coefficient of inbreeding (α) obtained for the three regions and for the whole Diocese of Taubaté. The time variation of α exhibits different patterns according to the geographical and social conditions of the region considered.

Discussion and Conclusions

Wahlund (1928) and *Dahlberg* (1929, 1938, 1947) studied theoretically the human populations using the island model and proposed the name genetic isolates for the human population units for which isolate sizes can be estimated from the rates of consanguineous marriages. *Wright* (1943, 1946, 1951) has taken quite a different approach using the concept of isolation by distance which depends on migration (dispersion) rates of the individuals. Since these two parameters are related the two methods should check one another in the actual investigation of human populations. However, both models introduce great simplifications in the enormous complexity of the demographical, cultural and social factors underlying the

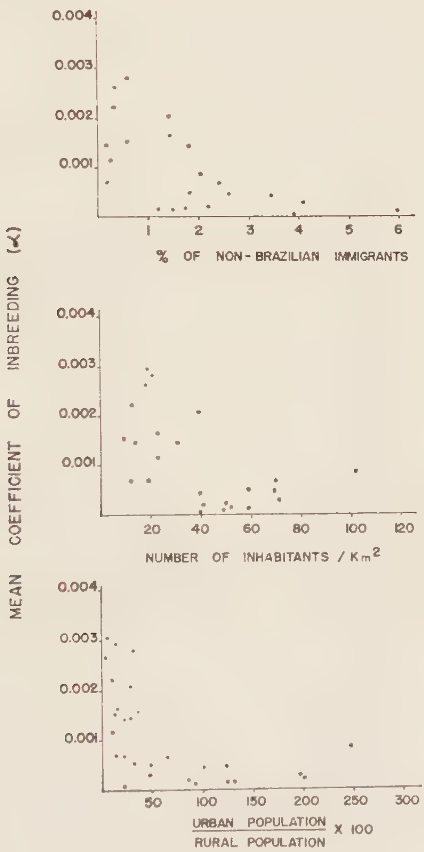

Fig. 4.
Association between mean coefficient of inbreeding and demographical factors.

Table 5. Frequencies of cousin marriages, mean coefficient of inbreeding, isolate sizes, population density, percent of non-Brazilian immigrants and relative urban population for 32 communities of the Northeast of São Paulo (Diocese of Taubaté), and for 6 communities of the Central part of the State of São Paulo (Diocese of Piracicaba)

Municipality	Parish (District)	Consanguinity						Demography (1)		
		Period	N	1 C (%)	CT (%)	$\alpha\ (\times 10^6)$	Isolate size	Population density	Percent of non-Brazilian immigrants	Urban pop. / Rural pop.
Natividade	N. S. de Natividade	1920–56	2,085	2.16	6.19	223	861	13.81	0.28	0.101
	N. S. Conceição (Bairro Alto)	1920–34	475	2.53	4.84	203	735	–	–	–
Redenção	Sta. Cruz	1920–51	1,493	2.21	7.23	264	841	18.22	0.28	0.057
S. Luiz	S. Luiz Tolosa	1920–55	3,615	1.69	3.46	144	1,100	14.13	0.14	0.220
Lagoinha (2)	N. S. Conceição	1920–55	1,890	2.91	8.25	294	639	18.49	–	0.129
Sta. Branca	Sta. Branca	1920–37	695	3.74	5.75	277	497	20.62	0.54	0.319
Salesópolis	S. José	1920–51	2,047	1.81	3.76	163	1,028	22.65	1.46	0.155
Paraibuna	Sto. António	1920–51	4,179	1.12	3.04	114	1,661	23.75	0.25	0.111
Jambeiro	N. S. das Dôres	1920–44	910	0.44	1.87	70	4,227	19.45	0.14	0.199
Taubaté	S. Francisco Chagas	1920–57	5,833	0.92	2.05	87	2,021	107.41	2.08	2.46
	N. S. do Rosário	1925–54	3,961	0.03	0.05	5	93,000	–	–	–
	Sma. Trindade	1948–56	794	0.00	0.00	–	–	–	–	–
	Imaculada Conceição (Quiririm)	1920–52	530	0.57	1.32	53	3,263		–	0.302
S. José dos Campos	S. José	1920–56	6,349	0.30	0.46	23	6,200	49.78	2.18	2.050
	S. Dimas	1951–57	400	0.00	0.00	–	–	–	–	–
	Santana	1935–57	1,740	0.63	1.38	57	2,952	–	–	–
Guaratinguetá	Sto. António	1920–57	6,066	0.18	0.35	14	10,333	56.21	1.22	1.313
	Pmo. Coração de Maria	1928–56	2,382	0.46	0.88	47	4,043	–	–	–

Jacareí	Imaculada Conceição	1920–56	5,823	0.57	1.08	46	3,263	69.20	2.60	1.239
	N. S. Sma. Trindade	1950–54	400	0.25	0.25	16	7,440	–	–	–
Pindamonhagaba	N. S. do Bom Sucesso	1920–27	5,366	0.22	0.45	18	8,454	40.59	1.70	0.864
	N. S. Assunção	1951–55	402	0.75	0.75	47	2,480	–	–	–
Caçapava	S. João Batista	1920–56	4,305	0.19	0.30	14	9,789	58.38	1.47	1.240
Tremembé	Bom Jesús	1920–58	1,782	0.67	1.07	50	2,776	57.65	1.82	0.494
Aparecida	Santana (Roseira)	1920–34	685	1.90	2.92	156	979	–	–	0.370
Campos do Jordão (3)	Sta. Terezinha	1923–55	1,722	0.17	0.23	12	10,941	47.78	5.98	0.926
S. Bento de Sapucaí	S. Bento Sapucaí	1920–55	2,881	2.66	4.58	209	699	38.42	1.43	0.263
	S. António do Pinhal	1920–54	1,302	1.31	3.00	118	1,419	–	–	–
Monteiro Lobato	N. S. Bom Sucesso	1920–57	1,508	1.99	3.51	155	935	9.85	0.60	1.130
Sta. Isabel	Sta. Isabel da Hungria	1920–56	2,548	1.37	4.00	146	1,358	30.43	1.82	0.272
Igaratá (2)	N. S. do Patrocínio	1920–37	667	0.90	1.65	70	2,067	12.15	–	0.132
S. José dos Campos	S. Francisco Xavier	1920–42	570	3.33	7.54	304	558	–	–	0.067
Piracicaba	Sto. Antonio	1920–55	8,111	0.30	0.60	26	6,200	62.75	4.09	1.976
Capivari	S. João Batista	1920–55	4,426	0.45	1.11	44	4,133	38.86	3.46	1.008
	N. S. Lourdes (Rafard)	1923–38	610	0.49	0.49	31	3,796	–	–	0.468
Sta. Barbara de Oeste	Sta. Barbara do Oeste	1920–54	3,044	0.79	1.71	69	2,354	69.67	2.43	0.636
Rio das Pedras	Senhor Bom Jesús	1928–47	1,200	0.08	0.08	5	23,250	38.96	3.81	0.220
S. Pedro	S. Pedro	1940–48	609	0.00	0.00	–	–	9.75	3.53	0.577

1. Data on population density from the Census of 1956 and data on percent of non-Brazilian immigrants and relative rural and urban populations from the General Census of 1950.
2. Elevated to the status of municipality after 1950.
3. Vacation and cure resort, 1600 m. high.

dynamics of human populations (for discussion see *Morton*, 1955). Boths models have been applied to some of the above communities but these results will be presented elsewhere.

Parishes, districts or other small geographical units are, in general, better isolated from each other than bigger units such as states or countries and therefore give a better understanding of the population dynamics. This fact has not been emphasized enough. From the above data the genetical structure of human populations appears to be varying considerably in time and for different locations. The increase of the geographical and social mobility of individuals also varied according to the regions studied. This must be caused by a set of variables, among which population density, percent of non-Brazilian immigrants and relative size of the urban population seem to be more important. Table 5 presents rates of cousin marriages (first cousin, total consanguinity, α value and isolate size) obtained for a similar period (1920–1957) as well as the demographical conditions of 32 parishes of the Diocese of Taubaté and of 6 parishes of the Diocese of Piracicaba. From these data the present great heterogeneity of the communities in the area investigated is apparent.

Table 6. Estimates and significance of correlations between mean coefficients of inbreedings or percent of first cousin marriages and demographical factors

	n	$r \pm S_r$	$z \pm S_z$	z/S_z	P
		Percent of non-Brasilian immigrants			
% 1 C	22	—0.596 ± 0.143	—0.645 ± 0.229	2.82	<0.01
α	22	—0.633 ± 0.128	—0.745 ± 0.229	3.25	<0.001
		Population density (no. inhabitants/km²)			
% 1 C	24	—0.510 ± 0.151	—0.562 ± 0.218	2.58	<0.01
α	24	—0.547 ± 0.143	—0.613 ± 0.218	2.81	<0.01
		Relative urban population (urban pop./rural pop. × 100)			
% 1 C	28	—0.511 ± 0.140	—0.563 ± 0.200	2.82	<0.01
α	28	—0.534 ± 0.135	—0.595 ± 0.200	2.96	≃ 0.001

n = number of parishes examined
$r \pm S_r$ = coefficient of correlation ± standard error
$z \pm S_z$ = corresponding z value ± standard error

Figure 4 shows an association between demographical factors and a values. The correlation between a and the percent of non-Brazilian immigrants, the population density and the relative size of the urban population was tested. The coefficients of correlation obtained for these demographical factors were negative (about –.5 to –.6) and the frequency of non-Brazilian immigrants, considered separately, seems to be the most effective factor. The negative correlations between demographical factors and a values or percent of first cousin marriages were statistically significant, being the association higher for a values than for frequencies of first cousin marriages (Table 6).

The isolation of the communities is related to each of the demographical factors considered here. The altitude of the communities has been taken by *Cavalli-Sforza* (1956) as a measure of the isolation of the populations in his investigation of the parishes belonging to the Diocese of Parma. A negative correlation between altitude of the community and the rates of consanguinity was detected. The data obtained by *Cavalli-Sforza* (1956) as well as the present data, make apparent the importance of ecological factors on the genetical structure of human populations.

Rising economical conditions promote the improvement and availability of the means of communication so that social factors outweigh the previously important ecological factors. As a general picture human populations are becoming more and more genetically homogeneous, even though the process is by no means uniform, as can be inferred from the present investigation.

Summary

Frequencies of cousin marriages in the northeast of the State of São Paulo, Brazil, were investigated. The area consists of three regions, a valley and two mountain chains, with different geographical and social conditions. The mean coefficient of inbreeding declined with time in the three regions, but this trend was more pronounced for the valley, which has been subject to strong internal immigrations and recent industrialization.

A significant negative correlation was found between the actual rates of inbreeding (a) and the demographical variables: percent of non-Brazilian immigrants, population density and relative urban population. The study of the population structure by parish units suggests that the populations are tending toward greater genetical homogeneity but the process is not uniform in the various parishes.

Zusammenfassung

Untersuchung von Verwandtenehen im Nordosten des Staates São Paulo ergab folgendes: Drei Gegenden dieses Gebietes mit verschiedenen geographischen und sozialen Bedingungen, nämlich zwei Bergketten und ein Tal, zeigten im Laufe der Zeit Abnahme der mittleren Inzucht-Koeffizienten, was in der Talgegend mit starker innerer Wanderung und jungen Industrien deutlicher war als in den Berggegenden. Die Korrelation zwischen den gegenwärtigen Inzuchtgeschwindigkeiten (α) und demographischen Variablen: wie Prozentsatz nichtbrasilianischer Einwanderer, Bevölkerungsdichte und Anteil der Stadtbevölkerung war eindeutig negativ. Das Studium der Bevölkerungsstruktur nach Kirchensprengeln läßt vermuten, daß sich die Bevölkerungen der gleichmäßigen Durchmischung nähern, doch verläuft dieser Prozeß in den drei Gegenden nicht mit gleicher Intensität.

Résumé

Nos recherches ont porté sur les marriages entre cousins dans la partie nord-est de l'Etat de São Paulo (Brésil). Ce territoire comporte trois régions; une vallée et deux chaînes de montagnes dont les conditions sociales et géographiques sont différentes. Le coefficient moyen de croisements consanguins décroît au cours du temps dans les trois régions, mais cette diminution s'observe davantage dans la vallée qui a été sujette à d'importantes immigrations internes et à une industrialisation récente. Nous avons observé une corrélation négative significative entre les taux de croisements consanguins (α) et les variables démographiques: pourcentage d'immigrants non Brésiliens, densité de population et population urbaine relative. L'étude de la structure de la population par paroisses suggère que les populations tendent vers une plus grande homogénéité génétique, mais ce processus n'est pas uniforme dans les différentes paroisses.

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ÜBER DIE HÄUFIGKEITSVERTEILUNG DER BLUTGRUPPEN IN DER SCHWEIZ

Von F. LEGRAIN

Die erste zusammenfassende Darstellung über die Häufigkeitsverteilung der AB0-Blutgruppen in der Schweiz stammt von *R. Schütz* (1). Dieser hat im Jahre 1946 unter Leitung von *A. Fonio* in seiner Dissertation 33 964 Blutgruppenbestimmungen von Angehörigen der Luftschutztruppe nach Bürgerorten aufgeschlüsselt. *H. Kaufmann* (2) veröffentlichte im Jahre 1952 eine nach Kantonen gegliederte Übersicht über die Häufigkeitsverteilung der AB0-Blutgruppen und des Rhesusfaktors D, wobei sie sich im wesentlichen auf das damalige Untersuchungsgut des Blutspendedienstes des SRK stützte. Ihre Arbeit enthält im weiteren eine vollständige Übersicht über sämtliche bis 1952 veröffentlichten Blutgruppenreihenuntersuchungen aus unserem Lande. Die umfassendste Arbeit dieser Art wurde 1956 von *S. Rosin* (3) veröffentlicht. Sie enthält eine eingehende, nach Bürgerorten aufgeschlüsselte statistische Auswertung von 275 664 AB0-Blutgruppenbestimmungen bei Wehrmännern, welche vom 1. Dezember 1944 bis zum 30. Juni 1945 Militärdienst geleistet hatten. Das Untersuchungsgut von *Rosin* umfaßt 6,8 Prozent der damaligen Schweizer Bevölkerung.

Den Anlaß für die vorliegende Arbeit gaben die in den Jahren 1953/54 bei den Bündner Walsern durchgeführten sero-anthropologischen Untersuchungen (4–6). Für die statistische Auswertung der bei den Walsern erhobenen Befunde wurden repräsentative gesamtschweizerische Durchschnittswerte der verschiedenen Blutgruppen benötigt. Da seit der Arbeit

von *H. Kaufmann* (2) das Untersuchungsgut des Blutspendedienstes des SRK in dieser Hinsicht nicht mehr ausgewertet worden war, haben wir uns die Aufgabe gestellt, auf Grund einer statistischen Analyse des Untersuchungsgutes des Zentrallaboratoriums des Blutspendedienstes des SRK in Bern und des ihm angeschlossenen Armeeblutgruppenlaboratoriums solche Durchschnittswerte zu ermitteln.

1. $A_1 A_2$ B0-Blutgruppensystem

Da die bis zum Jahre 1952 erhältlichen Angaben über die Häufigkeitsverteilung der AB0-Blutgruppen von *H. Kaufmann* (2) kritisch gesichtet wurden, erübrigt es sich, an dieser Stelle auf die früheren Arbeiten einzutreten. Die Arbeit von *H. Kaufmann* (2) umfaßt 91 784 Bestimmungen, von welchen 20 617 = 22,46% aus dem Zentrallaboratorium des Blutspendedienstes des SRK stammen. Wir haben diese 20 617 AB0-Bestimmungen in unser Material I einbezogen.

Unser Material setzt sich aus 86 294 AB0-Bestimmungen bei Blutspendern und 104 167 AB0-Bestimmungen bei Stellungspflichtigen zusammen. 10 457 Spender stammen aus der Stadt Bern. Der Rest stammt aus den verschiedenen regionalen Blutspendezentren unseres Landes. Die Mehrzahl der Spender ist in den ländlichen Gegenden des schweizerischen Mittellandes und den Voralpen beheimatet. Nur ein geringer Teil dieses Untersuchungsgutes stammt aus dem Jura, aus Gebirgskantonen oder aus dem Tessin. Im weiteren enthält das vorliegende Untersuchungsgut nur wenige Spender aus Basel, Zürich, Lausanne und Genf. Diese Städte verfügen über eigene, vom Zentrallaboratorium in bezug auf blutgruppenserologische Untersuchungen unabhängige Rot-Kreuz-Spendezentren, welche zudem, wegen des großen Vollblutbedarfes der städtischen Spitäler, ihr Spenderkorps dem Zentrallaboratorium für die Herstellung von Trockenplasma und Plasmafraktionen nicht zur Verfügung stellen können. Da im Armeeblutgruppenlaboratorium seit dem Jahre 1954 bei sämtlichen 19-jährigen Stellungspflichtigen des Landes AB0-Blutgruppenbestimmungen und Rhesusfaktorbestimmungen durchgeführt werden, erstreckt sich dieses Untersuchungsgut entsprechend der Bevölkerungsdichte auf das ganze Land.

Um auslesefrei zu sein, wurden bei dieser Erhebung ausschließlich Blutgruppenbestimmungen von Individuen mit unbekannter Blutgruppenzugehörigkeit verwertet. Die Auszählung wurde in zwei Etappen durchgeführt. Das Material I enthält 48 834 AB0-Bestimmungen bei Blutspendern, die vom 15. Juli 1949 bis zum 31. Juli 1954 in der serologischen Abteilung

des Zentrallaboratoriums durchgeführt worden waren. Es enthält im weiteren 23 959 AB0-Bestimmungen bei Stellungspflichtigen. Diese Bestimmungen wurden vom 1. April bis zum 31. Juli 1954 im Armeeblutgruppenlaboratorium vorgenommen. Dieses als Material I bezeichnete Untersuchungsgut diente der Arbeitsgemeinschaft für sero-anthropologische Untersuchungen bei den Bündner Walsern bei der statistischen Auswertung ihrer Bestimmungen als Vergleichsbasis. Gegen Ende des Jahres 1956 haben wir das seit dem 31. Juli 1954 angefallene Untersuchungsgut ausgezählt. Dieses nachstehend als Material II bezeichnete Untersuchungsgut enthält 37 460 Bestimmungen bei Blutspendern, die vom 1. August 1954 bis zum 30. November 1956 durchgeführt worden waren. Es enthält außerdem 80 208 AB0-Bestimmungen bei Stellungspflichtigen, die vom 1. August 1954 bis zum 31. Oktober 1956 untersucht worden waren. Aus äußeren Gründen hat sich die Fertigstellung dieser Arbeit bis ins Jahr 1960 hinausgezögert.

Die statistische Auswertung dieses 190 461 AB0-Bestimmungen umfassenden Untersuchungsgutes ergab folgendes:

Tabelle 1

Material	Zahl		0	A	B	AB	p	q	r	D/σ
I	72 793		29 938	34 143	6 005	2 687				
		%	41,16	46,90	8,25	3,69	29,71	6,16	64,13	—0,55
II	117 668		48 098	55 756	9 558	4 256				
		%	40,88	47,38	8,12	3,62	30,00	6,05	63,95	+0,34
Total	190 461		78 056	89 899	15 563	6 943				
		%	40,98	47,20	8,17	3,65	29,89	6,09	64,02	—0,05

Die Berechnung der Genhäufigkeiten im AB0-System wurde wie folgt durchgeführt:

Häufigkeit des A-Gens = p
Häufigkeit des B-Gens = q
Häufigkeit des 0-Gens = r

$$p = p' \left(1 + \frac{D}{2}\right)$$

$$q = q' \left(1 + \frac{D}{2}\right)$$

$$r = 1 - p - q \quad \text{wobei}$$

$$p' = 1 - \sqrt{\frac{B+0}{N}}; \qquad q' = 1 - \sqrt{\frac{A+0}{N}}; \qquad r' = \sqrt{\frac{0}{N}}$$

$$D = 1 - p' - q' - r' \qquad \sigma = \sqrt{\frac{pq}{2N(1-p)(1-q)}}$$

D/σ ist ein Maß für die innere Homogenität (Genotypengleichgewicht). $D/\sigma > 2$ kommt entweder bei stark heterogenem Material oder bei Bestimmungsfehlern zustande. Vergleiche *Mourant* (7) und *Rosin* (3).

Die beiden Untersuchungsreihen wurden mit der χ^2-Methode auf Homogenität geprüft. Ein gesicherter Unterschied zwischen dem Material I und dem Material II wurde nicht gefunden. χ^2 (3) = 4,6; P = 20%. Die innere Homogenität ist im Material I, II und im Total gut. $D/\sigma < 2$. Die beiden Untersuchungsreihen dürfen daher unbedenklich zu einem Gesamtmaterial vereinigt werden.

In der Arbeit von *Rosin* (3) zeigte sich ein systematisch wiederkehrendes Defizit von AB, das zu einer Inhomogenität im D/σ-Test führte. Da diese Abweichung im vorliegenden Material fehlt, ist mit praktischer Sicherheit anzunehmen, daß das im Untersuchungsgut von *Rosin* enthaltene AB-Defizit auf serologischen Bestimmungsfehlern beruhte. Daß dem so ist, ist auch aus den seinerzeitigen Untersuchungen von *R. Salber* (8) zu ersehen, welcher zeigte, daß bei den während der Mobilmachung 1939–1945 im Felde durchgeführten Blutgruppenbestimmungen oft die Blutgruppe A_2 in Kombination mit B nicht erfaßt wurde.

Bei 15 617 der 89 899 A-Individuen und bei 1228 der 6943 AB-Individuen wurde die A-Untergruppenzugehörigkeit ermittelt. Die Bestimmung wurde mit absorbierten B-(Anti-A_1) Seren durchgeführt. Absorptionsversuche wurden nur in seltenen Ausnahmefällen vorgenommen. Blutproben, die bei der einfachen Objektträgeragglutination mit Anti-A_1-Testseren nicht eindeutig als A_1 oder A_2 beziehungsweise A_1B oder A_2B identifiziert werden konnten, wurden als Intermediärformen klassiert und als A_i bezeichnet. Es ist anzunehmen, daß die meisten dieser sogenannten Intermediärformen bei eingehender Prüfung zum Beispiel durch Absorptionsversuche ebenfalls der einen oder andern A-Untergruppe hätten zugeordnet werden können.

Das Ergebnis der statistischen Auswertung der A_1/A_2-Bestimmungen ist aus den Tabellen 2 und 3 zu ersehen.

Tabelle 2

Material	Zahl		A_1	A_2	A_i	p_2/p	p_1	p_2
I	11 613		9 545	1 869	199			
		%	82,19	16,09	1,71			
ohne A_i	11 414	%	83,63	16,37	–	19,30	23,98	5,73
II	4 004		3 304	670	30			
		%	82,52	16,73	0,75			
ohne A_i	3 974	%	83,14	16,86	–	19,70	24,09	5,91
Total	15 617		12 849	2 539	229			
ohne A_i	15 388	%	83,50	16,50	–	19,49	24,07	5,82

Tabelle 3

Material	Zahl		A_1B	A_2B	A_iB	p_2/p
I	911		674	233	4	
ohne A_iB	907	%	74,31	25,69	–	25,69
II	317		225	89	3	
ohne A_iB	314	%	71,66	28,34	–	28,34
Total	1 228		899	322	7	
ohne A_iB	1 221	%	73,63	26,37	–	26,37

Die Berechnung der Häufigkeiten p_1 für das Gen A_1 und p_2 für das Gen A_2 geschieht unter Weglassen der Intermediärformen und unter Einbezug der Gesamthäufigkeit von 0 und A wie folgt *(Rosin)*:

$$\frac{p_2}{p} = \frac{\sqrt{0 + A\,\dfrac{A_2}{A_1 + A_2}} - \sqrt{0}}{\sqrt{0 + A} - \sqrt{0}}$$

Mit Hilfe von p aus Tabelle 1 kann nun p_1 und p_2 gefunden werden. Die Häufigkeiten p_1 und p_2 sind unabhängig von der großen Zahl der A_1- und A_2-Bestimmungen, auch direkt aus der viel geringeren Zahl der A_1B und A_2B zu berechnen. Das Verhältnis von p_1 und p_2 wird hier direkt durch das Verhältnis von A_1B und A_2B dargestellt.

Das in der Tabelle 2 zusammengestellte Material I + II zeigt eine stark gesicherte Differenz in A_i : χ^2 (1) = 19,5. P $\ll$ $1^0/_{00}$. Dies beruht offenbar

darauf, daß die in den ersten Jahren verwendeten Anti-A_1-Testseren gegenüber denjenigen der späteren Jahre qualitativ unterlegen waren. Dagegen besteht keine gesicherte Differenz für A_1 und A_2 ohne A_i : χ^2 (1) = 0,5. P = 50%.

Das in der Tabelle 3 enthaltene Material I und II zeigt keinen gesicherten Unterschied : χ^2 (1) = 0,8. P = 40%. Der an den AB-Untergruppen festgestellte Anteil der A_2-Gene ist aber ganz erheblich größer als derjenige, der an den Untergruppen von A berechnet wurde. Da die Gesamthäufigkeit von AB den Erwartungen entspricht, handelt es sich im vorliegenden Material um eine Verschiebung von A_1B zu A_2B. Diese Differenz beruht offensichtlich auf der Abschwächung der phänotypischen Ausprägung der Blutgruppe A in Anwesenheit von B. Es ist anzunehmen, daß eine nicht unerhebliche Zahl von A_2B-Blutproben dem Genotypus A_1B angehörten.

2. *Rhesusblutgruppensystem*

H. Kaufmann (2) hat als erste über die Häufigkeitsverteilung der Rhesusfaktoren in der Schweiz berichtet. Ihre Arbeit enthält 46 089 Bestimmungen des Rhesusfaktors D, von welchen 20 868 = 45,3% aus dem Zentrallaboratorium des Blutspendedienstes des SRK stammen. Wir haben diese 20 868 Bestimmungen in unser Material I einbezogen. In derselben Arbeit berichtete *H. Kaufmann* (2) erstmals über die Häufigkeitsverteilung der Rh-Untergruppen in der Schweiz, wobei sie sich auf das Material von *L. Holländer* (9), *A. Hässig* (10) und *R. Fischer* (11) stützte. Das Material von *A. Hässig* (10), welches 1095 Blutspender der Stadt Bern und 905 Spender aus der übrigen Schweiz umfaßte, wurde in unser Material I einbezogen. Hinsichtlich der Herkunft des Untersuchungsgutes verweisen wir auf den Abschnitt I über die A_1A_2B0-Blutgruppen.

Die Ergebnisse der statistischen Auswertung der 167 078 auf das Rhesusantigen D untersuchten Blutproben sind aus der Tabelle 4 zu ersehen.

Tabelle 4

Material	Zahl		D^+	D^-	d-Gene
I	63 217		52 587	10 630	
		%	83,18	16,82	41,01
II	103 861		86 456	17 405	
		%	83,24	16,76	40,94
Total	167 078		139 043	28 035	
		%	83,22	16,78	40,96

Die Häufigkeit der d-Gene entspricht der Wurzel von D^- der dd homozygot ist. Zwischen dem Material I und II wurde kein gesicherter Unterschied festgestellt : χ^2 (1) = 0,09. P = 75%. Die beiden Untersuchungs-

Tabelle 5

Material I	D^+-Untergruppe	% der D^+	D^--Untergruppe	% der D^-	%
CcDee	2 215	42,006			34,943
CCDee	1 266	24,009			19,972
CcDE	847	16,063			13,362
ccddee			5 790	92,300	15,520
ccDE	857	16,253			13,520
ccDee	69	1,309			1,089
Ccddee			283	4,511	0,759
CCDE	19	0,360			0,300
ccddE			183	2,917	0,491
CcddE			15	0,239	0,040
CCddee			2	0,032	0,005
CCddE			0		0,000
	5 273 = 83,185%	100,000	6 273 = 16,815%	99,999	100,001

Tabelle 6

Material II	D^+-Untergruppe	% der D^+	D^--Untergruppe	% der D^-	%
CcDee	1671	43,067			35,850
CCDee	902	23,247			19,351
CcDE	655	16,881			14,052
ccddee			3672	91,777	15,380
ccDE	583	15,026			12,508
ccDee	58	1,495			1,244
Ccddee			204	5,099	0,854
CCDE	11	0,284			0,236
ccddE			110	2,749	0,461
CcddE			13	0,325	0,054
CCddee			2	0,050	0,008
CCddE			0	0,000	0,000
	3880 = 83,242%	100,000	4001 = 16,758%	100,000	99,998

Tabelle 7

Gesamtmaterial	D^+-Untergruppe	% der D^+	D^--Untergruppe	% der D^-	%
CcDee	3886	42,456			35,332
CCDee	2168	23,686			19,711
CcDE	1502	16,410			13,656
ccddee			9462	92,097	15,454
ccDE	1440	15,733			13,093
ccDee	127	1,388			1,155
Ccddee			487	4,740	0,795
CCDE	30	0,328			0,273
ccddE			293	2,852	0,479
CcddE			28	0,273	0,046
CCddee			4	0,039	0,007
CCddE			0	0,000	0,000
	9153 = 83,220%	100,001	10 274 = 16,780%	100,001	100,001

reihen dürfen deswegen unbedenklich zu einem Gesamtmaterial vereinigt werden.

Da sich die Rh-Untergruppenbestimmung in der weit überwiegenden Mehrzahl der Fälle auf die Bestimmung der Antigene C, c und E beschränkte, haben wir uns bei der statistischen Auswertung auf die 4 Antigene C, c, D und E beschränkt. Aus dem auf Rh untersuchten Gesamtmaterial wurden bei 6,5% der Rh+- und bei 37% der Rh−-Blutproben die Antigene C, c und E bestimmt. Die in den Tabellen 5, 6 und 7 angegebenen Phänotypenhäufigkeiten wurden unter Berücksichtigung der unten in den Tabellen angegebenen Gesamthäufigkeiten für Rh+ und Rh− berechnet.

Die statistische Auswertung des in Tabelle 5 dargestellten Materials I und des in Tabelle 6 dargestellten Materials II ergab keine gesicherte Differenz. χ^2 für Rh+- und Rh−-Untergruppen getrennt geprüft und kombiniert: χ^2 (9) = 8,0, P > 50%. Das Material I und II durfte deswegen unbedenklich zu dem in Tabelle 7 dargestellten Gesamtmaterial vereinigt werden.

Die Berechnung der Rhesuschromosomenhäufigkeit erfolgte mit den von *Mourant* (7) angegebenen Formeln. Sie ergab folgendes:

R_1 CDe = 43,59%
r cde = 39,08%
R_2 cDE = 13,97%

Ro	cDe	= 1,43%
R′	Cde	= 1,02%
R″	cdE	= 0,61%
R_z	CDE	= 0,30%

Die aus dem Gesamtmaterial berechneten Genhäufigkeiten sind folgende:

C = 44,90%	c = 55,10%
D = 59,04%	d = 40,96%
E = 14,88%	e = 85,12%

3. MN-Blutgruppensystem

Als einziger hat 1952 *Läuppi* (12) anhand von 4225 forensischen MN-Bestimmungen des gerichtlich-medizinischen Institutes der Universität Zürich Angaben über die Häufigkeitsverteilung der MN-Faktoren in der Schweiz veröffentlicht.

Im Zentrallaboratorium des Blutspendedienstes des SRK wurden MN-Bestimmungen im allgemeinen nur bei forensischen Blutuntersuchungen (Vaterschaftsgutachten) durchgeführt. Das Material I enthält 3069 Bestimmungen aus der Zeit vom 15. Juli 1949 bis zum 31. Juli 1954. Das Material II enthält 3116 Bestimmungen aus der Zeit vom 1. August 1954 bis zum 30. November 1956. Es wurden lediglich die Bestimmungsergebnisse bei den unter sich nicht verwandten Individuen (Kindsmütter, fragliche Kindsväter und Mehrverkehrszeugen), nicht aber die Bestimmungsergebnisse bei den Kindern statistisch ausgewertet. Herkunftmäßig verteilt sich das Untersuchungsgut gleichmäßig auf die gesamte Schweiz.

Das Ergebnis der statistischen Auswertung ist aus der Tabelle 8 zu ersehen.

Tabelle 8

Material	Zahl		Phänotypen MM	Phänotypen MN	Phänotypen NN	Gene M	Gene N
I	3069		911	1495	663		
		%	29,68	48,71	21,60	54,04	45,96
II	3116		870	1608	638		
		%	27,92	51,60	20,48	53,72	46,28
Total	6185		1781	3103	1301		
		%	28,80	50,17	21,03	53,88	46,12

Die Häufigkeit der Gene wurde mit der «Genzählmethode» bestimmt:

$$M = \frac{2\ MM+MN}{2.\ Totalzahl}; \qquad N = \frac{2\ NN+MN}{2.\ Totalzahl}$$

Eine statistisch gesicherte Differenz zwischen dem Material I und II wurde nicht gefunden: χ^2 (1) = 0,1. P = 60%. Die innere Homogenität ist beim Material I gut (χ^2 = 1,15. P = 28%), beim Material II fraglich (χ^2 = 4,37. P = 3,7%), beim Gesamtmaterial gut (χ^2 = 0,55. P = 47%).

Reihenuntersuchungen über die Häufigkeit der Antigene S und s fehlen derzeit in unserem Lande.

4. P-Blutgruppensystem

Im Zentrallaboratorium des Blutspendedienstes des SRK wurden vom 15. Juli 1949 bis zum 30. November 1956 vorwiegend bei forensischen Blutuntersuchungen bei 732 unter sich nicht verwandten Individuen Bestimmungen des P-Faktors durchgeführt.

Das Ergebnis der statistischen Auswertung dieses Untersuchungsgutes ist aus der Tabelle 9 zu ersehen.

Tabelle 9

P	Zahl		P+	P –	p-Gene
	732		585	147	
		%	79,92	20,08	44,81

5. Kell-Blutgruppensystem

Im Zentrallaboratorium des Blutspendedienstes des SRK wurden seit dem 26. Juli 1952 K-Bestimmungen routinemäßig bei forensischen Blutuntersuchungen durchgeführt (13, 14). Das in der Tabelle 10 aufgeführte Material I stammt aus der Zeit vom 26. Juli 1952 bis zum 31. Juli 1954. Das Material II stammt aus der Zeit vom 1. August 1954 bis zum 29. Mai 1956. Hinsichtlich der Auswahl und Herkunft der Blutproben verweisen wir auf den Abschnitt 3 über die MN-Faktoren.

Das Ergebnis der statistischen Auswertung ist aus der Tabelle 10 zu ersehen:

Tabelle 10

Material	Zahl		K+	K⁻	k-Gene
I	1256		93	1163	
		%	7,40	92,60	96,23
II	1417		111	1306	
		%	7,83	92,17	96,01
Total	2673		204	2469	
		%	7,63	92,37	96,11

Zwischen dem Material I und dem Material II besteht keine statistisch gesicherte Differenz: χ^3 (1) = 0,2. P = 65%.

6. *Duffy-Blutgruppensystem*

L. Holländer (15) hat 1951 Angaben über die Häufigkeit des Blutgruppenantigens Fy^a in der Basler Bevölkerung veröffentlicht. Seit dem 26. Juli 1952 wurden im Zentrallaboratorium des Blutspendedienstes des SRK bei forensischen Blutuntersuchungen routinemäßig Fy^a-Bestimmungen durchgeführt (13, 14). Das in der Tabelle 11 aufgeführte Material I stammt aus der Zeit vom 26. Juli 1952 bis zum 31. Juli 1954; das Material II stammt aus der Zeit vom 1. August 1954 bis zum 29. Mai 1956. Hinsichtlich Auswahl und Herkunft der Blutproben verweisen wir auf den Abschnitt 3 über die MN-Faktoren.

Das Ergebnis der statistischen Auswertung ist aus der Tabelle 11 zu ersehen:

Tabelle 11

Material	Zahl		Fy(a+)	Fy(a−)	Fy^b-Gene
I	1137		748	389	
		%	65,79	34,21	58,49
II	1417		927	490	
		%	65,42	34,58	58,80
Total	2554		1675	879	
		%	65,58	34,42	58,67

Zwischen dem Material I und dem Material II besteht kein statistisch gesicherter Unterschied: χ^2 (1) = 0,02. P ~90%.

7. *Lewis-Blutgruppensystem*

A. Hässig, W. Meyer und *D. Thommen* (16) haben 1955 bei 1000 unter sich nicht verwandten Blutspendern der Blutgruppe 0, die sich herkunftsmäßig über die ganze Schweiz verteilten, Bestimmungen der Faktoren Le^a und Le^b durchgeführt. Das Ergebnis dieser Untersuchung ist aus der Tabelle 12 zu ersehen.

Tabelle 12

Lewis	Zahl		Le(a+b–)	Le(a–b+)	Le(a–b–)
	1000		213	651	136
		%	21,3	65,1	13,6

Da die Genetik des Lewis-Blutgruppensystems noch nicht restlos klar ist, mußten wir auf die Berechnung von Genhäufigkeiten verzichten.

8. *Lutheran-Blutgruppensystem*

R. Gonzenbach, A. Hässig und *S. Rosin* (17) sowie *L. Holländer* (18) haben im Jahre 1955 über Untersuchungen über die Genhäufigkeit der Gene Lu^a und Lu^b in der Schweiz berichtet.

Das Ergebnis ihrer Untersuchungen ist aus der Tabelle 13 zu ersehen:

Tabelle 13

Lutheran	Zahl		Lu(a+)	Lu(a–)	Lu^b - Gene
	1208		65	1143	
		%	5,38	94,62	97,27

9. *Kidd-Blutgruppensystem*

G. Halle, A. Hässig und *S. Rosin* (19) haben im Jahre 1955 bei 1000 unter sich nicht verwandten rhesusnegativen Individuen der Blutgruppe 0 Jk^a-Bestimmungen vorgenommen. Die Blutproben stammten aus dem

Armee-Blutgruppenlaboratorium und verteilten sich herkunftsmäßig gleichmäßig auf die gesamte Schweiz.

Das Ergebnis ihrer Untersuchungen ist aus der Tabelle 14 zu ersehen:

Tabelle 14

Kidd	Zahl		Jk(a+)	Jk(a−)	Jk^b - Gene
	1000		783	217	
		%	78,30	21,70	46,58

Zusammenfassung

Anhand einer statistischen Auswertung des Untersuchungsgutes des Zentrallaboratoriums des Blutspendedienstes des SRK in Bern aus den Jahren 1949–1956 wurden repräsentative Zahlen bezüglich der Häufigkeitsverteilungen der Antigene der A_1A_2B0-, Rhesus-, MN-, P-, Kell-, Duffy-, Lewis-, Lutheran- und Kidd-Blutgruppensysteme ermittelt. Die ermittelten Genfrequenzen können als Grundlage für genetische, forensische und anthropologische Blutgruppenuntersuchungen in der Schweiz dienen.

Summary

The blood group distribution in Switzerland has been studied by means of a material collected and tested by the Swiss Red Cross Blood Transfusion Service in Bern during the years 1949–1956.

Résumé

En se basant sur le matériel du laboratoire central du Centre de transfusion de la Croix-Rouge suisse à Berne, concernant les années 1949–1956, on a pu obtenir une statistique significative en ce qui concerne la fréquence des antigènes des systèmes sanguins (A_1A_2B0, Rhesus, MN, P; Kell, Duffy, Lewis, Lutheran et Kidd). Les fréquences des gênes ainsi établies peuvent servir de base pour des recherches génétiques médico-légales et anthropologiques des groupes sanguins en Suisse.

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DAS PAPILLARLEISTENSYSTEM DER HAND UND SEINE BEZIEHUNG ZU CEREBRALEN STÖRUNGEN[1]

Von WALTER HIRSCH und GEORG GEIPEL

Es gibt im medizinischen Schrifttum eine Reihe von Versuchen, zwischen den von den Papillarleisten in der Handfläche geformten Mustern sowie dem Verlauf der Hauptlinien einerseits und cerebralen Störungen andererseits Beziehungen aufzudecken. Diese Untersuchungen sind allerdings nicht so häufig wie die Arbeiten, die nach Veränderungen des Papillarleistensystems auf den Fingerkuppen bei cerebralen Störungen gesucht haben. Die meisten derartigen Untersuchungen betrafen zunächst gar nicht das Papillarsystem der Hand, sondern das zweite, gröbere Liniennetz der Hand, das als Handfurchensystem bezeichnet wird und von alters her das Hauptfeld der Handdeutung oder Chiromantik darstellt. Der Grund hierfür liegt darin, daß das Auftreten einer Vierfingerfurche (Affenfurche, Sperrfurche) bereits 1909 vom Sohne des ersten Beschreibers der mongoloiden Idiotie,

[1] *Herrn Professor Dr. Dr. h. c. Hans Nachtsheim zum 70. Geburtstag am 13. Juni 1960.*

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R. L. Langdon-Down, als mongoloides Merkmal von diagnostischer Bedeutung erkannt worden war. Bei der Vierfingerfurche (Abb. 11, 12) findet sich bekanntlich an Stelle der beiden großen Furchen der distalen Innenhand, der sogenannten Dreifingerfurche und Fünffingerfurche, nur eine einzige Furche, die die Innenhand quer durchzieht und sie dadurch in einen distalen und proximalen Abschnitt zerlegt. Bei der mongoloiden Idiotie beschränkt sich die Anomalie nicht auf die Vierfingerfurche allein, sondern es weichen auch die Papillarleisten von der Norm ab: Es findet sich nämlich häufigere Musterbildung in den Interdigitalräumen II und III, geringere Musterbildung im Interdigitalraum IV und auf dem Thenar als bei normalen Menschen. Außerdem haben die Hauptlinien bei der mongoloiden Idiotie einen mehr transversalen Verlauf, der in der Endigung der Hauptlinie D in 13 (5% gegen 1% Norm) und in 11 (2/3 der Fälle gegen 1/3 Norm) zum Ausdruck kommt. Die axialen Triradien t sind bei der mongoloiden Idiotie mehr distal gelagert als bei der Normalbevölkerung: Verbindet man den am meisten distal gelegenen Triradius t mit den Triradien a und d, so kommt ein Winkel zustande, der bei 83,7% der Mongoloiden über 57 Grad beträgt, während nur 7,9% Normale einen Winkel über 57 Grad aufweisen. – Zu diesen Messungen von *Penrose* paßt auch die Angabe, daß bei der Vierfingerfurche der weit distal gelegene axiale Triradius t'' allein und in der Kombination tt'' und t't''t^u bei Individuen mit Vierfingerfurche relativ häufig ist, die Bemusterung von Thenar und Hypothenar als normal bezeichnet wird (im Gegensatz zu der oben angeführten geringeren Bemusterung des Thenars bei Mongoloiden). Im Zusammenhang mit dem transversalen Verlauf der Hauptlinien hatte schon *Cummins* große Hypothenarmuster mit distalen Triradien bei Mongoloiden festgestellt.

Im Rahmen von genetisch-klinischen Untersuchungen an anomalen und cerebral geschädigten Kindern hatten wir 1957 auch die Handleisten untersucht, wobei wir im ganzen 190 Personen, Eltern und Kinder, untersuchten, von denen 75 einen organischen Hirnschaden aufwiesen und 69 infolge Milieuschadens eine neurotische Fehlentwicklung ohne nachweisbare organische Veränderungen zeigten, während 46 als normale Kontrollen dienten. Von statistisch gesicherten Ergebnissen sei aus dieser Publikation erwähnt, daß die C-Linie bei den Kindern mit neurotischer Fehlentwicklung viermal häufiger fehlte als bei den normalen Vergleichspersonen, und daß die gleiche Gruppe auch im Vergleich zu den Normalpersonen häufiger (17,4% gegen 34,8%) ein von Sekundärfurchen und Querfalten beherrschtes Bild ihrer Innenhand darbot.

Diese Ergebnisse sowie die Tatsache, daß das Papillarleisten- und Furchenbild der Handfläche, abgesehen von der mongoloiden Idiotie, bei cere-

bralen Schäden wenig untersucht worden ist, haben uns ermutigt, das Papillarleistensystem und die Furchung der Hand an einem größeren Krankengut zu untersuchen. Wir wählten das Kindersanatorium «Wiesengrund», ein zum Bezirksamt Reinickendorf des Senats von Berlin gehörendes Kinderheim, und die Kinderabteilung der Städtischen Heilstätten in Berlin-Wittenau, in denen wir 289 anomale Kinder im Alter von 3 bis 16 Jahren (207 männliche, 82 weibliche) untersuchten. Das starke Überwiegen des männlichen Geschlechts in derartigen Heimen ist eine Erfahrungstatsache, deren Ursache noch nicht aufgeklärt ist. Der Erklärungsversuch, daß abnormale Mädchen leichter im häuslichen Milieu zu halten seien oder daß die Familien am Schicksal der Söhne mehr interessiert und daher leichter mit einem Heimaufenthalt einverstanden seien, stimmt jedenfalls bei unserem Krankengut nicht.

Von 289 Patienten (207 ♂♂, 82 ♀♀) konnten Stammbäume angefertigt werden bei

224 Patienten (165 ♂♂, 59 ♀♀). Von diesen 224 Familien sind in

65 Familien die Patienten einzige Kinder (51 ♂♂, 14 ♀♀). Es verbleiben

159 Familien mit 114 ♂♂ und 45 ♀♀ Patienten. Von diesen sind in

38 Familien mehrere cerebral geschädigte Kinder vorhanden, von denen aber nur eins pro Familie als Patient in der Anstalt untersucht wurde. 2 bis 7 cerebral geschädigte Kinder pro Familie kamen in diesen

38 Familien vor (73 ♂♂, 29 ♀♀). In diesen Familien waren außerdem noch 29 ♂♂ und 29 ♀♀ gesunde Geburten vorhanden.

Das Verhältnis von ♂♂ zu ♀♀ ist also in allen diesen Fällen 2,5 zu 1 oder sogar noch höher. Vor allem ist wichtig, daß auch bei denjenigen der 38 Familien, in denen mehrere cerebral geschädigte Kinder vorhanden sind, das Verhältnis von 2,5 ♂♂ zu 1 ♀ besteht, daß also nicht etwa mehr cerebral geschädigte ♀♀ zu Hause gehalten werden. Ermittelt man dagegen die Zahl der gesunden Geschwister aller Familien, so findet man 139 ♂♂ und 151 ♀♀, also fast die gleiche Anzahl. Aus diesen Zahlen geht hervor, daß jedenfalls unter unserem Krankengut 2½mal soviel ♂♂ von cerebralen Schäden betroffen waren als ♀♀.

Das von uns bearbeitete Krankengut ist insofern einheitlich, als bei allen Kindern *mindestens eine* angeborene, genetisch oder frühfötal bedingte Anlage für ihre abwegige psychische und intellektuelle Entwicklung angenommen werden konnte. Kinder, bei denen die cerebrale Störung durch grob mechanische Schäden im letzten Drittel der Schwangerschaft oder kurz vor, bei oder nach der Geburt bedingt war, wurden zwar untersucht, aber

bei der statistischen Bearbeitung nicht berücksichtigt, weil die Bildung der Papillarleisten im 5. Embryonalmonat abgeschlossen ist, die Muster später nicht mehr veränderlich sind und daher spätere Schäden keinen Einfluss auf das Tastleistensystem haben können. – Außerdem wurden Mongoloide nicht einbezogen, weil die Abweichungen im Papillarleistensystem bei dieser Krankheit bekannt sind und es uns darauf ankam, nach Beziehungen zwischen Papillarleisten und solchen cerebralen Schäden zu suchen, bei denen noch keine sicheren Ergebnisse vorliegen. – Dagegen wurden außer den sicher genetisch bedingten oder früh embryonal entstandenen cerebralen Erkrankungen auch frühkindliche Hirnschäden und neurotische Fehlentwicklungen bei Milieuschäden in die Untersuchung einbezogen, weil bei diesen eine abwegige Anlage vorliegen kann: Es ist häufig auch genetisch bedingt, ob eine frühkindliche Infektion zu einer cerebralen Komplikation führt oder nicht. Bei unserem Krankengut sprechen jedenfalls bereits die oben angeführten Zahlen über die Patientenfamilien für eine solche Auffassung.

Bei den von uns untersuchten Kindern lassen sich 3 Hauptgruppen unterscheiden:

1. Geistig defekte Kinder mit organischem Hirnschaden genetischer oder infektiöser Ursache. Zu dieser Gruppe gehören die angeborenen Stoffwechselabweichungen («inborn errors of metabolism»).

2. Milieuschäden mit neurotischer Fehlentwicklung und Psychopathie.

3. Geistiger Entwicklungsrückstand unbekannter Ursache («mental retardation of unknown origin»). «das buntdurchwürfelte Syndrom oder sogar das Symptom der Oligophrenie» *(Richterich)*.

In dieser Gruppe, zu der die negativen Extremvarianten der Normalbevölkerung gehören, hat die genetisch-biochemische Forschung eine Reihe von Krankheitsbildern ätiologisch als intermediäre Stoffwechselstörungen aufgeklärt. Sie kommen hier nicht in Betracht. Diese Gruppe ist immer noch die größte der geistigen Fehl- und Unterentwicklung.

Diese 3 Hauptgruppen verflechten sich in vielfältiger Weise. Ein geistig defektes Kind wird zum Beispiel auf eine Schädigung durch das Milieu leichter mit einem Milieuschaden, etwa neurotischer Fehlentwicklung, reagieren als ein normales. Andererseits kann ein Milieuschaden einen Entwicklungsrückstand sowohl vortäuschen als auch einen tatsächlichen vorhandenen Entwicklungsrückstand verschlimmern. (Keine der bekannten «chemisch verursachten Mißbildungen» wurde bei unseren Patienten gefunden.)

Obwohl über den Verlauf der Hauptlinien, die Musterhäufigkeit und die Musterverteilung der Hand bei verschiedenen Populationen Mitteilungen

vorliegen, und obwohl für die Interpretation und die Formulierung der palmaren Dermatoglyphen seit dem Erscheinen der «revised methods» (1929) von *Cummins und Mitarbeiter* international einheitliche Gesichtspunkte verfolgt werden, war es notwendig, Kontrolluntersuchungen bei gesunden Populationen vorzunehmen. Schon die allgemein anerkannte Bezeichnung «Interpretation» für die Untersuchung des Tastleistensystems zeigt, daß subjektive Einflüsse auf das Ergebnis trotz aller Bemühung nicht ganz zu vermeiden sind. Die Untersuchung der Patienteneltern und Patientengeschwister war deshalb unzureichend, weil, wie oben verzeichnet, in einer Reihe von Familien (38) mehrere cerebral geschädigte Kinder vorhanden waren und auch die Eltern (die Mütter in 45 Familien) in ihrer geistigen Entwicklung nicht als durchaus normal bezeichnet werden konnten. Dagegen waren die Patienten von der allgemeinen Berliner Population nur durch das Vorliegen eines cerebralen Schadens unterschieden. – Als Vergleichspopulation dienten zunächst Berliner Zwillinge (83 ♂♂, 104 ♀♀), wobei von jedem Paar natürlich nur einer herangezogen wurde. – Als zweite Vergleichspopulation dienten 600 normale Individuen (300 ♂♂, 300 ♀♀), die uns von Prof. *G. G. Wendt* in Marburg Lahn zur Verfügung gestellt wurde. Hierbei handelt es sich um gesunde Deutsche aus verschiedenen Teilen des Bundesgebietes, vorwiegend aus Hessen.

Das Arbeitsprogramm für die Untersuchung der palmaren Dermatoglyphen umfaßte die folgenden 8 Punkte:

1. Hypothenarmuster, Art und Häufigkeit,
2. Thenarmuster, Art und Häufigkeit,
3. Axiale Triradien, $tt't''t^{u}$, Häufigkeit,
4. Interdigitalmuster, Art und Häufigkeit,
5. Modaltypen (Hauptlinienendigungskombinationen),
6. Kombinationen von Thenar und Hypothenarmustern,
7. Bemusterung der Hände, Musterzahl je Hand und Person,
8. Handfurchung (die 3 Stufen nach *Tillner*).

Die Handleistenbilder und ihre Bezeichnungen

Die Abb. 2 und 3 zeigen den Abdruck einer Hand, die unterhalb der Finger II, III, IV, V die Triradien a, b, c, d erkennen lassen. Von jedem dieser Triradien läuft eine Leiste nach der Handfläche, die als Hauptlinie A, B, C, D bezeichnet wird. Zum Zwecke der Abgrenzung werden die verschiedenen Bereiche der Handfläche am Handrande mit arabischen Ziffern 1–13 bezeichnet. Außer den genannten Triradien a–d treten auf der

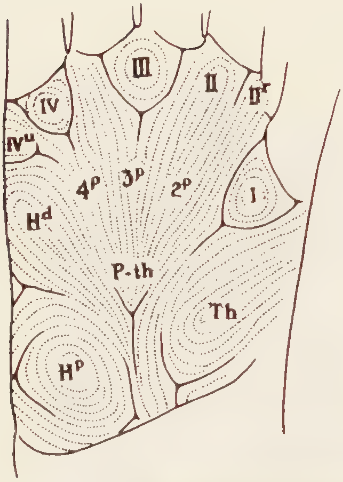


Abb. 1

Der Grundplan der Primatenhand, proximal die Interdigitalräume (IR) I bis IV, distal Hypothenar und Thenar, zwischen ihnen der proximale oder axiale Triradius P-th oder t. Die Ballen, die Triradien und die von ihnen umschlossenen Muster sind eingezeichnet (nach *Midlo* und *Cummins*).

Abb. 2

Normale menschliche Hand, in die der proximale oder axiale Triradius t, die distalen Triradien a, b, c, d und die von diesen ausgehenden Hauptlinien A, B, C, D, sowie Muster in den IR II, III, IV und auf dem Hypothenar eingezeichnet sind. Die Handabschnitte sind von 1 bis 13 beziffert (nach *Geipel*).

Handfläche nahe ihrer Längsmittelachse oft noch «achsiale Triradien» auf, die von proximal nach distal als t, t′, t″ oder, falls mehr ulnarwärts gelegen, als tu bezeichnet werden (Abb. 5). - Diese Punkte und Linien können Leistenmuster in den Interdigitalbezirken, auf dem Thenar und Hypothenar umformen, die – ähnlich denen der Fingerbeere – als Bogen (B), Schleifen (L) und Wirbel (W) oder, falls es sich nicht um ausgeprägte Muster, sondern nur um Musterspuren, «vestiges», handelt, als V bezeichnet werden, während ein musterfreier Bezirk als «offenes Feld» mit 0 (Null) angegeben wird. Die Bogen und Schleifen auf Hypothenar und Thenar erhalten je nach ihrem radialen, ulnaren oder carpalen Auslauf die Bezeichnung A^r (arch), A^u, A^c, L^r (loop), L^u, L^c. – Die Handflächenformel beginnt mit den Hauptlinien D. C. B. A. nennt aber nur die Endigungsstellen mit ihren arabischen Ziffern am Handrande, also zum Beispiel 11.9.7.5. Es folgen die achsialen Triradien (etwa tt′ t^u), und anschließend die Muster oder die musterfreien Felder von Hypothenar, Thenar, II, III, IV (also etwa L^u. L^c/L^r.0.L.0).

1. *Hypothenarmuster, Art und Häufigkeit* (Abb. 3, 8, 9, 10)

Bei der Bezeichnung und Berechnung der Hypothenarmuster sind hier ausnahmsweise zwei Vereinfachungen vorgenommen worden. Erstens ist der ulnare, offene Hypothenarbogen A^u zu den «offenen Feldern» gerechnet und als 0 bezeichnet worden (Abb. 3). Der Unterschied ist in der Tat sowohl morphologisch wie auch grundsätzlich unbedeutend. Zweitens ist darauf verzichtet worden, beim Vorliegen eines t′ den distalen und den proximalen Hypothenarteil getrennt zu bezeichnen und für den proximalen Abschnitt stets ein A^c anzunehmen, weil durch das Verzeichnen von t′ die Trennung des Hypothenars in einen distalen und proximalen Abschnitt bereits genügend gekennzeichnet ist (Abb. 8).

Bei der Aufzeichnung der Muster kann zwischen einfachen und zusammengesetzten Mustern (Kombinationen) unterschieden werden. Die Zahl der überhaupt vorkommenden einfachen Muster ist bei den Wiesengrund- und Wittenau-Patienten (P) die gleiche wie bei den beiden Normalpopulationen, den Berliner Zwillingen (Z) und der Marburger Bevölkerung (M), nämlich:

einfache Hypothenarmuster	P	= 8
	Z	8
	M	= 9

Dagegen zeigt ein Blick auf die Tabelle, daß bei P das Musterbild bunter ist:

7 . 5″. 5′. 1–t–A[u]–0–0–0–L

Abb. 3

Die Bezirke des Handrandes zur Bezeichnung der Hauptlinienendigungen sind mit arabischen Ziffern 1 bis 13 beschriftet. – Papillarleistensysteme: keine Muster (bis auf eine Schleife in IR IV), sondern freie Felder. Ein axialer Triradius: t. Furchensystem: Außer den drei Hauptfurchen zahlreiche Sekundär- oder Querfurchen (Furchungsgrad 3 nach *Tillner)*.

kombinierte Hypothenarmuster P = 23
Z = 16
M = 15

Die Gesamtzahl der überhaupt vorkommenden Hypothenarmuster ist also:

Gesamtzahl der Hypothenarmuster P = 31
Z = 24
M = 24

$9 \cdot 7 \cdot 5'' \cdot 5'\text{-t} \quad L^r \cdot 0 \cdot m \cdot 0 \cdot L$

Abb. 4

Auf dem Hypothenar und in IR IV eine Schleife, sonst musterfreie Felder. Ein axialer Triradius t. Geringes Furchungssystem (Furchungsgrad 2 nach *Tillner).*

Es besteht bei den drei Populationen kein Unterschied in der Musterzahl auf rechten und linken Händen, also kein Rechtslinksunterschied.

In bezug auf die Geschlechter ist bei Z und M nur eine Tendenz zu größerer Musterhäufigkeit bei ♀♀ zu verzeichnen, also besteht kein gesicherter Geschlechtsunterschied.

Musterhäufigkeit von ♂ und ♀ (in % aller Hände) bei

	♂♂	♀♀
P	71,26	71,34
Z	48,79	59,13
M	45,83	51,00

Tabelle 2

Handmuster Hypothenar

	Beob.-wert	Erwartungs-wert	χ^2	Beob.-wert	Erwartungs-wert	χ^2	Summe
	Wiesengrund-Patienten			Berliner Zwillinge			
		P			Z		P+Z
einfache Muster	345	293,40	9,07	178	229,60	11,60	523
zusammenges. Muster	67	52,17	3,82	26	40,83	5,39	93
musterfreie Felder	66	132,40	33,30	170	103,60	42,56	236
	478	56,10%		374	43,90%		852
		$\chi^2_{(2)} = 105{,}74$			$p < 10^{-10}$		
				Marburger Normalbevölkerung			
		P			M		P+M
einfache Muster	345	247,86	38,07	525	622,14	15,17	870
zusammenges. Muster	67	34,19	31,85	53	85,81	12,69	120
musterfreie Felder	66	196,01	86,22	622	491,99	34,35	688
	478	28,49%		1200	71,51%		1678
		$\chi^2_{(2)} = 218{,}35$			$p < 10^{-10}$		
		M			Z		M+Z
einfache Muster	525	535,97	0,22	178	167,03	0,72	703
zusammenges. Muster	53	60,23	0,87	26	18,77	2,78	79
musterfreie Felder	622	603,82	0,54	170	188,18	1,72	792
	1200	76,24%		374	23,76%		1571
		$\chi^2_{(2)} = 6{,}85$			$p = 0{,}033$		
		P		Patientenfamilien (F)			P+F
einfache Muster	345	312,80	3,31	233	255,20	4,06	568
zusammenges. Muster	67	64,98	0,06	51	53,02	0,08	118
musterfreie Felder	66	100,23	18,41	116	81,77	14,33	182
	478	55,07%		390	44,93%		868
		$\chi^2_{(2)} = 40{,}25$			$p = 10^{-9}$		

Aus diesen Zahlen geht bereits hervor, daß die Musterhäufigkeit auf dem Hypothenar bei den Patienten (P) erheblich größer ist als bei den beiden Normalpopulationen (Z und M). Die statistische Auswertung (Tab. 2) erfolgte nach dem χ2-Verfahren, wobei bei jeder Population [illegible] und [illegible], rechts und links zusammengefaßt, die Anzahl der einfachen Muster, der zusammengesetzten Muster und der musterfreien Felder verzeichnet und P gegen Z, P gegen M, M gegen Z verglichen wurden. Die Berechnung ergab für P gegen Z und für P gegen M eine ungewöhnlich hohe statistische Sicherung mit einem $p < 10^{-10}$! Hierbei sind beide Normalpopulationen von

Tabelle 3

Handmuster Hypothenar
Patientenfamilien gegen die beiden Normalbevölkerungen

	Beob.-wert	Erwartungs-wert	χ^2	Beob.-wert	Erwartungs-wert	χ^2	Summe
	Patientenfamilien (F)			Berliner Zwillinge (Z)			
einfache Muster	223	204,71	1,58	178	196,29	1,65	401
zusammenges. Muster	51	39,31	3,69	26	37,69	3,79	77
musterfreie Felder	116	146,00	6,16	170	140,00	6,43	286
	390	51,05%		374	48,95%		764
		$\chi^2_{(2)} = 23{,}30$			$p = 10^{-5}$		
	F			Marburger Normalbevölkerung (M)			
einfache Muster	223	183,48	19,67	525	564,52	2,70	748
zusammenges. Muster	51	25,51	24,04	53	78,49	8,01	104
musterfreie Felder	116	181,03	23,34	622	556,97	7,58	738
	390	24,53%		1200	75,47%		1595
		$\chi^2_{(2)} = 85{,}43$			$p = 10^{-10}$		

den Patienten in gleicher Richtung unterschieden, indem die Patienten mehr einfache Muster, mehr zusammengesetzte Muster und daher auch weniger musterfreie Felder aufweisen.[1]

Die beiden Normalpopulationen unterscheiden sich voneinander mit einem $p = 0{,}033$, also einer sehr geringen statistischen Sicherung, indem Z etwas mehr Muster und entsprechend weniger freie Felder aufweist als M. Daß Normalpopulationen in bezug auf ihre Dermatoglyphen voneinander unterschieden sind, ist allgemein bekannt. Es ist aber immer wieder wichtig, solche Schwankungen festzulegen. In unserem Falle spielen allerdings die leichten Unterschiede gegenüber den Patienten angesichts der ungewöhnlich großen Sicherung der Unterschiede beider Normalpopulationen keine Rolle.

Bei 195 Patienten-Eltern und Geschwistern (nicht identisch mit den 224 Familien, bei denen vollständige Stammbäume vorliegen, siehe Seite 105) lagen Finger- und Handabdrücke vor. Ein Vergleich dieser Patientenfamilien mit den Patienten ergab einen statistisch gesicherten Unterschied in bezug auf die Hypothenarbemusterung von $p = 10^{-9}$, indem die Familien weniger einfache Muster und mehr musterfreie Felder am Hypo-

[1] Wegen der bekannten Korrelation zwischen den beiden *Händen* einer Person wird die Signifikanz dieser Ergebnisse überschätzt. Jedoch auch der Vergleich zwischen *Personen* in bezug auf Vorkommen und Fehlen von Mustern hat ein hoch signifikantes Ergebnis (S. 124 [6] und S. 127 [7] und Tabelle 9 und 10).

thenar haben als die Patienten (Tab. 3). Die Patientenfamilien stehen also in der Mitte zwischen den Patienten und den Normalbevölkerungen. Das zeigt sich auch, wenn die Familien (F) gegen Z und M verglichen werden. F unterscheidet sich zwar sowohl von Z wie von M mit einer hohen statistischen Sicherung, aber die Unterschiede sind doch erheblich geringer als die von P gegen Z und M:

χ^2 Werte von P und F gegen Z und M

P gegen Z = 105,74
F gegen Z = 23,30
P gegen M = 218,35
F gegen M = 85,34

Dieses Ergebnis bestätigt unsere Erwartung, da, wie bereits erwähnt, die Patientenfamilien keine Normalbevölkerung darstellen, sondern außer den Patienten auch unter den Eltern und Geschwistern weit mehr cerebral abwegige Individuen zu finden sind als in der Normalbevölkerung.

Zusammenfassend ist also festzustellen, daß bei unseren cerebral geschädigten Kindern eine weit stärkere, statistisch hoch gesicherte Bemusterung des Hypothenars vorliegt als bei 2 Normalbevölkerungen. Sowohl einfache wie zusammengesetzte Muster sind bei den Patienten häufiger, während die Zahl der musterfreien Felder bei den Patienten entsprechend geringer ausfällt. Zugleich ist das Bild bei den Patienten «bunter», indem eine größere Variation in der Ausgestaltung der zusammengesetzten Muster vorhanden ist. Schließlich ist zu vermerken, daß bei den Patienten in bezug auf die Musterhäufigkeit kein Geschlechtsunterschied besteht, während bei den Normalbevölkerungen die Muster bei ♀♀ überwiegen.

2. Thenarmuster, Art und Häufigkeit. (Abb. 6 und 10)

Genau wie beim Hypothenar ist auch beim Thenar zwischen einfachen und zusammengesetzten Mustern unterschieden worden. Die Tabelle zeigt, daß zwar die Zahl der einfachen Muster bei den Patienten (P = 7) gegenüber den beiden Normalbevölkerungen überwiegt (Z = 4; M = 4), daß aber von einem «bunteren» Bild bei P am Thenar – im Gegensatz zum Hypothenar – nicht gesprochen werden kann. Die Unterschiede zwischen den beiden Normalbevölkerungen zeigen hier vielmehr, wie vorsichtig man bei der Bewertung von Unterschieden sein muß, weil Variationen zwischen Normalbevölkerungen bestehen und zu berücksichtigen sind. Bei allen 3 Populationen ist ein Überwiegen von links zu verzeichnen, am stärksten bei P, nämlich 12,81%.

$11 \cdot X \cdot 7 \cdot 5' \; t'_1 t'_2 t'_3 t'' t^u \; L^r \; L^u \cdot V \cdot 0 \cdot 0 \cdot d$,

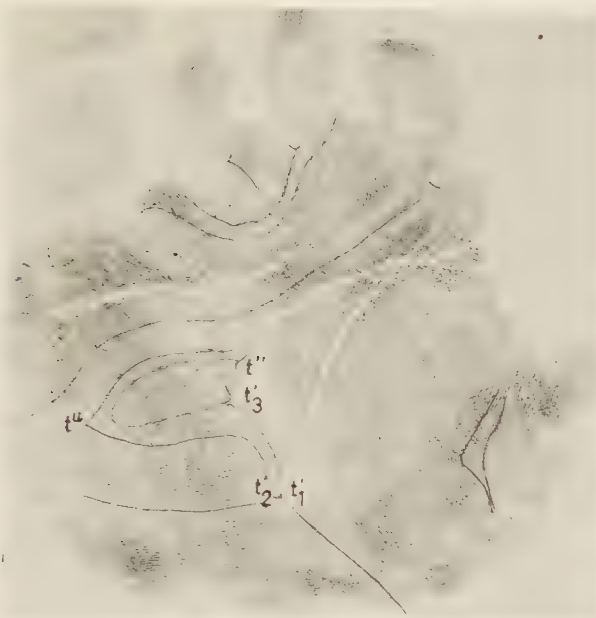


Abb. 5

Fünf axiale Triradien eingezeichnet – zwei Schleifenmuster auf dem Hypothenar –, dazu ein Spurenmuster V auf dem Thenar. Furchungsgrad 3.

Wichtig ist, daß - genau wie beim Hypothenar – ein Geschlechtsunterschied besteht, allerdings nicht bei den Patienten, sondern bei den beiden Normalpopulationen, und zwar ein Überwiegen des weiblichen Geschlechts.

Vergleich von P, Z, M in bezug auf die Thenar-Musterhäufigkeit bei ♂♂ und ♀♀ (Zahl der Hände dividiert durch die Zahl der Muster)

	♂♂	♀♀
P	3,57	3,35
Z	5,35	6,93
M	6,90	8,57

Der wichtigste und maßgebende Befund besteht aber genau wie am Hypothenar in der weitaus größeren Musterhäufigkeit und dem entsprechend selteneren Vorkommen musterfreier Felder bei den Patienten (P) im Vergleich zu den beiden Normalbevölkerungen (Z und M). Die Auswertung erfolgte wiederum nach dem $\chi 2$-Verfahren, wobei einfache Muster,

$7 \cdot 5'' \cdot 5' \cdot 4\text{–}tt'_1t'_2t^u_1t^u_2\text{–}L^r/W$ (Dsch) $\cdot 0 \cdot 0 \cdot 0 \cdot$ L

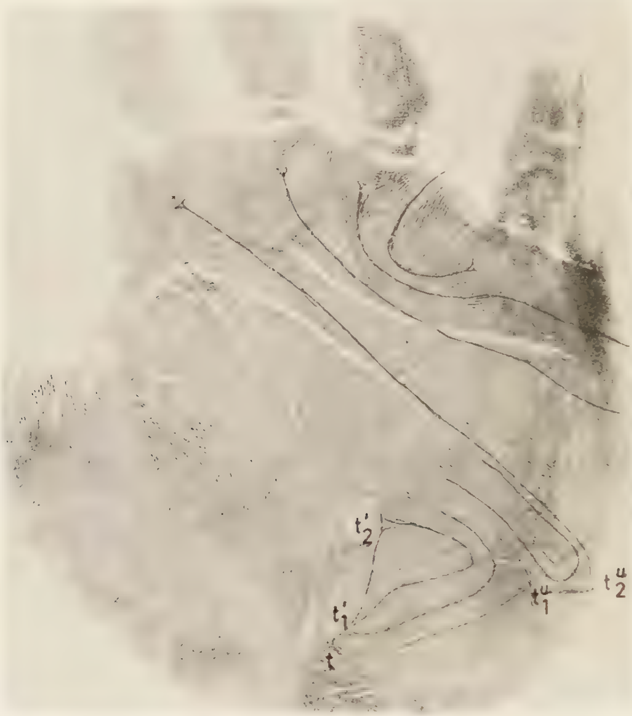


Abb. 6

Fünf axiale Triradien – auf dem Hypothenar eine Schleife und ein Wirbel –, in IR IV ein Schleifenmuster. Sekundärfurchung mittleren Grades (Furchungsgrad 2).

zusammengesetzte Muster und musterfreie Felder bei den verschiedenen Populationen miteinander verglichen wurden. Es ergab sich eine sehr hohe statistische Sicherung von $10^{-5,5}$ für p bei P gegen Z, und ein noch kleineres $p < 10^{-10}$ bei P gegen M. Die Abweichung der beiden Normalbevölkerungen gegen die Patienten erfolgt in der gleichen Richtung, indem beide Normalbevölkerungen weniger Muster und mehr musterfreie Felder am Thenar aufweisen als die Patienten.

Auf der anderen Seite ergibt der Vergleich der beiden Normalbevölkerungen untereinander den geringen Unterschied von $p = 0,04$, der die üblichen Schwankungen zwischen normalen Bevölkerungsgruppen zum Ausdruck bringt, die sich jedoch den Patienten gegenüber wie eine einheitliche Gruppe verhalten. Die Wiesengrundfamilien sind in bezug auf ihre Thenarmuster bei einem $p = 0,11$ mit den Wiesengrundpatienten identisch.

Zum Verständnis dieses Ergebnisses sei auf die bereits erwähnte Tatsache hingewiesen, daß sich unter den Eltern und Geschwistern der Patienten eine nicht geringe Zahl von cerebral abwegigen Personen befindet.

Die häufigere Bemusterung des Thenar bei den Patienten betrifft vor allem die einfachen Muster, indem nach carpal oder radial gerichtete Schleifen, Wirbel und deutliche Spurenmuster bei den Patienten so viel häufiger auftreten und dadurch die Häufigkeit eines musterfreien Thenar entsprechend herabsetzen. Dagegen ist das Vorkommen zusammengesetzter Muster, also der aus 3 Figurenmustern, einer radialen Schleife, einer Querfigur und einer carpalen Schleife zusammengesetzten sogenannten Bettmannschen Figur bei den 3 Populationen nicht wesentlich voneinander

Tabelle 4

Handmuster Thenar

	Beob.-wert	Erwartungs-wert	χ^2	Beob.-wert	Erwartungs-wert	χ^2	Summe
		Patienten (P)			Zwillinge (Z)		
einfache Muster	103	77,71	8,23	25	50,28	12,71	128
zusammenges. Muster	62	59,50	0,10	36	38,49	0,16	98
musterfreie Felder	431	440,75	175	313	285,17	2,72	726
	578	60,71%		374	39,28%		952
		$\chi^2_{(2)} = 25,67$			$p = 10^{-5,5}$		
		Patienten (P)			Marburg (M)		
einfache Muster	103	50,06	56,18	51	103,93	27,00	154
zusammenges. Muster	62	54,29	1,09	105	112,71	0,53	167
musterfreie Felder	413	473,67	7,61	1044	983,33	3,66	1457
	578	32.51		1200	67,49		1778
		$\chi^2_{(2)} = 96,07$			$p = 10^{-10}$		
		Marburg (M)			Zwillinge (Z)		
einfache Muster	51	57,94	0,83	25	18,06	2,72	76
zusammenges. Muster	105	107,50	0,06	36	53,50	0,19	141
musterfreie Felder	1044	1034,58	0,09	313	322,42	0,27	1357
	1200	76,24%		374	23,76%		1574
		$\chi^2_{(2)} = 4,16$			$p = 0,04$		
		Patienten (P)			Patientenfamilien (F)		
einfache Muster	103	100,81	0,05	66	68,19	0,07	169
zusammenges. Muster	62	55,47	0,77	31	37,53	1,14	93
musterfreie Felder	413	421,73	0,18	294	285,27	0,27	707
	578	59,65%		391	40,35%		969
		$\chi^2_{(2)} = 2,48$			$p = 0,11$		

unterschieden. Wir verzeichnen hier zunächst nur diese auffallende Tatsache, daß die volle Manifestation der Bettmannschen Figur bei den cerebral Geschädigten nicht höher ist als bei den beiden Normalbevölkerungen, und daß die sehr großen, statistisch hoch gesicherten Unterschiede nur das Auftreten von einfachen Mustern und von sicheren Spurenmustern auf dem Thenar betreffen, wodurch eben musterfreie Thenarfelder bei den Patienten so viel seltener werden.

3. Achsiale Triradien, tt′ t″ t^u, Häufigkeit (Abb. 4, 5, 6)

An den meisten Handflächen findet sich nahe der carpo-palmaren Grenze an der mit der arabischen Ziffer 2 bezeichneten Stelle, also auf der Handachse zwischen dem Thenar und Hypothenarballen, der als t bezeichnete Triradius (Tab. 5). Wie alle Triradien ist auch t dadurch charakterisiert, daß an ihm als Verzweigungspunkt 3 Leistenströme aneinander vorüberziehen (Tab. 6). Falls an dieser Stelle nur 2 Leistenströme vorhanden sind, weil der carpale Areus fehlt, wird der Verzweigungspunkt als p («Parting») bezeichnet. An Stelle von t oder zusätzlich zu t können distalwärts oder ulnarwärts Triradien auftreten, die von proximal nach distal die Bezeichnung t′, t″, t^u, unter Umständen je nach ihrer Lage auch t_1 t_2 t'_1 t'_2 erhalten.

Bei einem Vergleich der 3 Tabellen fällt zunächst auf, daß die Patienten ein «bunteres» Bild ihrer Triradien aufweisen, indem sie 32 verschiedene Kombinationstypen ihrer achsialen und ulnaren Triradien besitzen gegen 22 bei den Zwillingen (Z) und 26 bei der Marburger Normalbevölkerung (M). Diese vielfältigere Kombination betrifft lediglich diejenigen Hände, die 3 oder mehr achsiale Triadien haben: Bei den Patienten sind 17, bei Z 8 und bei M 9 solche Kombinationen verzeichnet.

Teilt man die 3 Populationen in 3 Gruppen ein, nämlich Personen mit einem, mit zwei und mit drei oder mehr achsialen Triradien, so ist zu fragen, wie die Verteilung rechts und links bei ♂ und ♀ ist. Bei der prozentualen Berechnung stellt sich heraus, daß die Unterschiede bei den 3 Populationen im wesentlichen als gleiche oder sehr ähnliche Schwankungen und zwar in der gleichen Richtung verlaufen. In bezug auf rechte und linke Hände sind die Ergebnisse insofern auffallend, als bei der Gruppe mit 1 Triradius zwar linke Hände häufiger betroffen sind, bei den Gruppen mit 2 oder 3 oder mehr Triradien aber rechte Hände in der Mehrzahl erscheinen. Auch hinsichtlich der Geschlechter sind Unterschiede deutlich, indem unter den Personen mit 1 Triradius die männlichen, unter den Gruppen mit 2 oder 3 oder mehr Triradien die weiblichen überwiegen. Es bestehen also sowohl Seiten- als auch Geschlechtsunterschiede und

müssen verzeichnet werden, obwohl sie für unsere Fragestellung irrelevant sind, indem die Schwankungen aller Populationen nach der gleichen Richtung verlaufen. Es muß aber eins hervorgehoben werden: Bei unseren Patienten wurden, wie oben geschildert, erheblich mehr ♂♂ als ♀♀ untersucht.

	♂♂	♀♀
P	72%	28%
Z	44%	56%
M	50%	50%

Bei gleichem Verhalten der Bevölkerung hätte man also eine geringere Bemusterung bei den Patienten erwarten müssen. Die Tatsache, daß trotz

Tabelle 5

Achsiale Triradien

Einteilung in 3 Gruppen mit 1, mit 2 und mit 3 oder mehr Triradien. Vergleich der Unterschiede von rechten und linken Händen, von ♂ und ♀ bei den 3 Populationen, den Patienten (P), den Berliner Zwillingen (Z) und der Marburger Bevölkerung (M).

		♂ rechts	♂ links	♀ rechts	♀ links	♂ r+l	♀ r+l
				mit 1 Triradius			
P	abs. Zahl	130	126	36	43	256	79
	%	62,80	60,87	43,90	52,44	61,84	48,17
Z	abs. Zahl	59	65	61	75	124	136
	%	71,08	78,31	58,09	71,43	74,70	64,76
M	abs. Zahl	204	216	179	208	420	378
	%	68,00	72,00	59,67	69,33	70,00	64,50
				mit 2 Triradien			
P	abs. Zahl	51	67	35	32	118	67
	%	24,64	32,37	42,68	39,02	28,50	40,85
Z	abs. Zahl	20	15	39	27	35	66
	%	24,10	18,07	37,14	25,71	21,08	31,43
M	abs. Zahl	82	74	104	79	156	183
	%	27,33	24,67	34,67	26,33	26,00	30,50
				mit 3 oder mehr achsialen Triradien			
P	abs. Zahl	26	14	11	7	40	18
	%	12,56	6,75	23,17	8,54	9,66	10,98
Z	abs. Zahl	4	3	5	3	7	8
	%		–	–	–	–	–
M	abs. Zahl	12	10	21	11	22	32
	%	4,00	3,33	7,00	3,67	3,67	5,33

Tabelle 6

Achsiale Triradien

Einteilung in 3 Gruppen, Personen mit 1, mit 2 und mit 3 oder mehr achsialen Triradien und Vergleich dieser 3 Gruppen in den 3 Populationen P, Z und M

	Beob.-wert	Erwartungs-wert	χ^2	Beob.-wert	Erwartungs-wert	χ^2	Summe
		P			Z		
1 Triradius	335	360,51	1,80	260	234,49	2,77	595
2 Triradien	185	173,29	0,79	101	112,71	1,22	286
3 oder mehr Triradien	58	44,23	4,29	15	28,77	6,59	73
	578	60,59%		376	39,41%		954
	$\chi^2_{(2)} = 17,46$					$p = 0,0002$	
		P			M		
1 Triradius	335	372,81	3,83	810	772,19	1,85	1145
2 Triradien	185	168,66	1,43	333	349.34	0,76	518
3 oder mehr Triradien	58	36,47	12,71	54	75,53	6,14	112
	578	32,56%		1197	67,44%		1775
	$\chi^2_{(2)} = 26,72$					$p = 10^{-6}$	
		Z			M		
1 Triradius	260	255.73	0.07	810	814.27	0.02	1070
2 Triradien	101	103.73	0,07	333	330.27	0.02	434
3 oder mehr Triradien	15	16.49	0.13	54	52.51	0.04	69
	376	23,90%		1197	76,10%		1573
	$\chi^2_{(2)} = 0,35$					$p = 0,7$	

der geringeren Zahl an . ; die Bemusterung bei den Patienten größer war, verstärkt also noch den Wert unserer Ergebnisse.

Bei der statistischen Auswertung stellte sich heraus, daß die beiden Normalbevölkerungen in bezug auf die Zahl ihrer achsialen Triadien identisch sind, mit einem $p = 0,7$. Dagegen sind beide Normalbevölkerungen von den Patienten in der gleichen Richtung unterschieden, indem bei den Patienten Personen mit nur einem achsialen Triradius seltener sind, dagegen sind Patienten mit 2 Triradien häufiger, und Patienten mit 3 oder mehr Triradien noch weitaus häufiger. Die Unterschiede sind hoch gesichert, P gegen Z mit $p = 0,0002$ und P gegen M mit $p = 10^{-6}$. (Hände, nicht Personen wurden verglichen; siehe Fußnote Seite 113)

4. *Interdigitalmuster, Art und Häufigkeit* (Abb. 7, 8, 10).

Die unterhalb der Fingerwurzel gelegenen sogenannten digitalen Triradien zeigen distalwärts je 2 Radianten, die die digitale Area oder Fläche

$11 \cdot 9 \cdot 7 \cdot 5'$–$tt^u$–$L^r \cdot 0 \cdot 0 \cdot L \cdot 0$

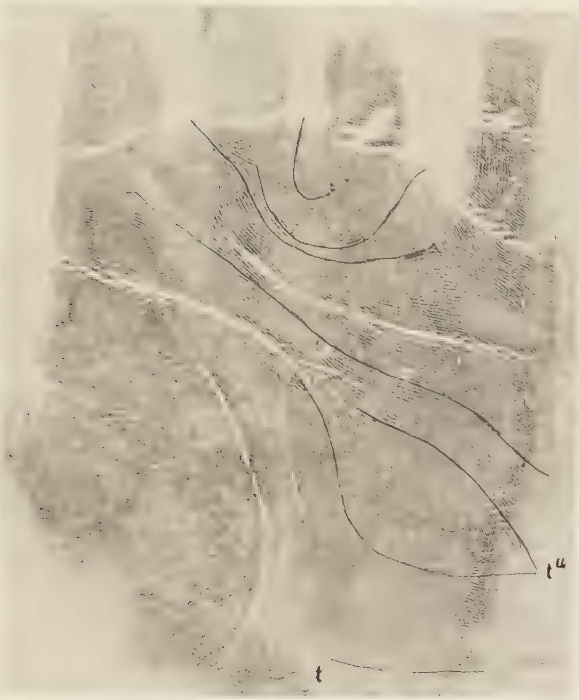


Abb. 7

Auf dem Hypothenar und in IR III eine Schleife, sonst musterfreie Felder – zwei axiale Triradien (häufiger Befund) –, Furchungssystem: keine Sekundärfurchen (Furchungsgrad 1).

einschließen. Zwischen diesen digitalen Triradien und ihren Radianten liegen die Interdigitalräume (IR) II, III und IV, deren Musterbildung wir bei unseren 3 Populationen miteinander vergleichen. Die verschiedenen Muster sind in den Tabellen in ihren Einzelheiten verzeichnet, doch konnte bei der statistischen Auswertung nur die Zahl der musterhaltigen gegen die musterfreien Felder verglichen werden.

In bezug auf Rechts-Links-Differenzen verhalten sich alle 3 Populationen gleich, indem im II. und im III. IR die rechten Hände, im IV. IR dagegen die linken Hände stärker bemustert sind. Unterschiede in der Bemusterung männlicher und weiblicher Hände sollten in der Tabelle eingesehen werden. Im II. IR sind bei allen 3 Populationen die ♂♂ stärker mit Muster versehen als die ♀♀. Im III. und IV. IR dagegen sind auch die Schwankungen zwischen den beiden Normalpopulationen so beträchtlich, daß keine grund-

sätzlichen Unterschiede daraus abgeleitet werden können. Man kann nur feststellen, daß in diesen Interdigitalräumen die Schwankungen zwischen ♂♂ und ♀♀ bald größer, bald kleiner sein können, und daß anscheinend zufallsmäßig einmal ♂♂ und einmal ♀♀ in bezug auf die Bemusterung überwiegen können.

Diese Schwankungen setzen bereits den Wert von statistischen Auswertungen herab, bei denen rechts und links, ♂♂ und ♀♀ zusammengefaßt werden und dann die 3 Populationen in bezug auf musterhaltige und musterfreie Felder verglichen werden. Auch sind die tatsächlichen statistischen Unterschiede bei weitem nicht so groß wie bei den bisher betrachteten Handbezirken: Im II. IR sind die beiden Normalpopulationen mit einem $p = 0{,}6$ identisch. Die Patienten weisen gegen die Zwillinge mit einem $p\ \ 0{,}05$ einen an der Grenze der statistischen Sicherung befindlichen Wert auf. Gegen die Marburger Bevölkerung sind die Patienten mit einem p $0{,}001$ einwandfrei unterschieden. Die Unterschiede bewegen sich bei P gegen Z und bei P gegen M so, daß die Patienten im II. IR häufiger Muster und entsprechend seltener musterfreie Felder aufweisen als die beiden Vergleichspopulationen.

Ähnliche Verhältnisse, allerdings mit noch geringerer statistischer Sicherung ergeben sich im IR III. P ist gegen Z mit einem $p = 0{,}045$ an der Grenze statistischer Sicherung. P ist gegen M mit einem $p = 0{,}12$ nicht mehr statistisch gesichert. Da aber Z und M identisch sind ($p = 0{,}95$), konnte man M + Z gegen P prüfen. Das Ergebnis ist mit $p = 0{,}07$ noch nicht statistisch gesichert. Immerhin sei erwähnt, daß die Unterschiede in der gleichen Richtung verlaufen, daß also auch im IR III. bei den Patienten allem Anschein nach mindestens eine Tendenz zu stärkerer Bemusterung und einer geringeren Ausbildung von freien Feldern besteht.

Im IV. IR verhalten sich alle 3 Populationen in bezug auf Muster und freie Felder identisch.

Zusammenfassend läßt sich sagen, daß in den Interdigitalräumen II und III eine Tendenz zu häufigerer Bemusterung und seltenerer Ausbildung freier Felder bei unseren Patienten im Vergleich zu 2 Normalpopulationen zu verzeichnen ist. Diese Unterschiede sind aber nicht immer statistisch gesichert.

5. *Hauptlinienendigungskombinationen* (Modaltypen)

Im Verlauf und den Endigungspunkten der 4 Hauptlinien A, B, C und D ist bei B 7 häufiger, 5′ seltener, bei C X und 0 seltener, bei D 10 und 8 häufiger als bei M und Z. Da die Streuungen zwischen M und Z sehr hoch

Tabelle 7

Muster und musterfreie Felder

Interdigitalraum II (IR II)

	Beob.-wert	Erwartungs-wert	χ^2	Beob.-wert	Erwartungs-wert	χ^2	Summe
		P			Z		
IR II Muster	60	51,60	1,37	25	33,40	2,11	85
IR II musterfrei	518	526,36	0,13	349	340,60	0,21	867
	578	60,71%		374	39,29%		952
	$\chi^2_{(1)}$ = 3.82				p = 0,05		
		P			M		
IR II Muster	60	40,96	8,85	66	85,04	4,27	126
IR II musterfrei	518	537,10	0,68	1134	1114,93	0,33	1652
	578	32,51%		1200	67,49%		1778
	$\chi^2_{(1)}$ = 14.13				p = 0,001		
		M			Z		
IR II Muster	66	69,38	0,16	25	21,62	0,53	91
IR II musterfrei	1134	1130,64	0	349	352,36	0,03	1483
	1200	76,24%		374	23,76%		1574
	$\chi^2_{(1)}$ = 0,72				p = 0,6		
		Interdigitalraum III (IR III)					
		P			Z		
IR III Muster	264	248,91	0,90	146	161,09	1,40	410
IR III musterfrei	314	329,05	0,68	228	212,95	1,06	542
	578	60,71%		374	39,29%		952
	$\chi^2_{(1)}$ = 4,04				p = 0,045		
		P			M		
IR III Muster	264	249,68	0,82	504	518,32	0,45	768
IR III musterfrei	314	328,35	0,63	696	681,65	0,30	1010
	578	32,51%		1200	67,49%		1778
	$\chi^2_{(1)}$ = 2,20				p = 0,12		
		P			M+Z		
IR III Muster	264	245,50	1,39	650	668,50	0,51	914
IR III musterfrei	314	332,53	1,03	924	905,47	0,38	1238
	578	2,86%		1574	73,14%		2152
	$\chi^2_{(1)}$ = 3.31				p = 0,07		
		Z			M		
IR III Muster	146	154,44	0,46	504	495,56	0,14	650
IR III musterfrei	228	219,54	0,19	696	704,46	0,10	924
	374	23,76%		1200	76,24%		1574
	$\chi^2_{(1)}$ = 0,89				p = 0,95		

sind, können diese Unterschiede trotz statistischer Sicherung nur als Hinweise gelten.[1]

Der Index nach *H. Cummins* ist für P 8,52, Z 8,18 und für M 8,37 (Abb. 2 und 3).

Tabelle 8

Interdigitalraum (IR) II/III/IV, Muster
♂ und ♀ getrennt, in absoluten Zahlen und in %, bei P, Z und M

		II IR		III IR		IV IR	
	Muster %	11,59	7,32	44,69	48,17	63,28	53,66
P	Muster abs. Zahl	48	12	185	79	262	88
	n	414	164	414	164	414	164
	Muster %	10,24	3,85	35,54	41,83	65,06	63,46
Z	Muster abs. Zahl	17	8	59	87	108	132
	n	166	208	166	208	166	208
	Muster %	7,33	3,67	46,17	37,83	58,00	64,83
M	Muster abs. Zahl	44	22	277	227	348	389
	n	600	600	600	600	600	600

6. Kombinationen von Thenar und Hypothenarmustern (Abb. 5, 7, 9, 10)

Nachdem sich die höhere Bemusterung von Hypothenar und Thenar bei den Patienten herausgestellt hatte (siehe Punkte 1 und 2), stellten die Berechnungen zu dieser Fragestellung nichts grundsätzlich Neues dar, sondern sie sind lediglich eine Erweiterung und Bestätigung der bereits bekannten Tatsachen. Wenn man die möglichen Musterkombinationen pro Patient an Hypothenar und Thenar zusammenfaßt, so ergeben sich pro Patient 4 Musterfelder mit 9 möglichen Kombinationen, die von Hypothenar (+), Thenar (+) bis zu Hypothenar (–), Thenar (–) reichen, wobei (+) natürlich musterhaltige und (–) musterfreie Felder bezeichnet. Die einzelnen Kombinationsmöglichkeiten sind aus der Tabelle 9 ersichtlich. Es wurde also bei den 3 Populationen P, Z und M für jede der 9 möglichen Musterkombinationen die Zahl der Patienten verzeichnet, die die betreffende Musterkombination besitzen, und dann wurden diese Zahlen miteinander verglichen, P gegen Z, P gegen M und M gegen Z. Hierbei zeigte sich

[1] Die rechnerischen Unterlagen können auf Verlangen vom Institut erhalten werden.

11·9·7·5′–t′–0·0·0·L·0

Abb. 8

Ein axialer Triradius, weiter distal als üblich, daher t′, oberhalb dessen ulnarem Schenkel die Leisten absteigen. Übliche Bezeichnung des distalen Abschnittes 0, des proximalen A^c. In unseren Statistiken ist diese Musterkombination zu den freien Feldern gerechnet worden. Furchungsgrad 2.

zunächst, daß die beiden Normalpopulationen Z und M in bezug auf die Häufigkeit der verschiedenen Musterkombinationen mit einem $p = 0{,}26$ identisch sind. Dagegen sind die Unterschiede beider Normalpopulationen gegenüber den Patienten statistisch hoch gesichert, P gegen Z mit $p < 10^{-6}$ und P gegen M mit $p < 10^{-10}$. Die Abweichungen vollziehen sich für jede einzelne der 9 Musterkombinationen bei Z und M gegenüber P

Tabelle 9

Thenar und Hypothenar — Musterkombinationen pro Person

		Beob.-wert	Erwartungs-wert	χ^2	Beob.-wert	Erwartungs-wert	χ^2	Σ
			P			Z		
Hyp + —	Th — —	37	46,75	2,03	40	30,25	3,14	77
+ +	— —	94	94,71	0	62	61,29	0	156
+ +	+ —	51	38,85	3,80	13	25,15	5,87	64
+ —	+ —	18	14,57	0,81	6	9,43	1,25	24
— —	+ —	9	10,93	0,34	9	7,07	0,53	18
— —	+ +	5	9,71	2,28	11	6,29	3,53	16
+ +	+ +	28	19,43	3,77	4	12,57	5,84	32
+ —	+ +	11	7,28	1,90	1	4,71	2,92	12
— —	— —	36	46,75	2,47	41	30,25	3,82	77
		289	60,71%		187	39,29%		476
			$\chi^2_{(8)} = 44,30$				$p = 10^{-6}$	
			P			M		
Hyp + —	Th — —	37	51,02	3,84	120	105,96	1,85	157
+ +	— —	94	88,40	0,35	178	183,57	0,17	272
+ +	+ —	51	25,02	27,04	26	51,97	13,00	77
+ —	+ —	18	12,02	3,00	19	24,97	1,44	37
— —	+ —	9	13,32	1,40	32	27,67	0,68	41
— —	+ +	5	7,80	1,00	19	16,20	0,48	24
+ +	+ +	28	13,32	16,18	13	27,67	7,78	41
+ —	+ +	11	6,17	3,78	8	12,82	1,81	19
— —	— —	36	71,82	17,86	185	149,15	8,62	221
		289	32,50%		600	67,49%		889
			$\chi^2_{(8)} = 110,28$				$p = < 10^{-10}$	
			M			Z		
Hyp + —	Th — —	120	121,98	0	40	38,02	0	160
+ +	— —	178	182,98	0,13	62	57,02	0,43	240
+ +	+ —	26	29,73	0,47	13	9,27	1,58	39
+ —	+ —	19	19,06	0	6	5,94	0	25
— —	+ —	32	31,26	0	9	9,74	0	41
— —	+ +	19	22,87	0,65	11	7,13	2,10	30
+ +	+ +	13	12,96	0	4	4,04	0	17
+ —	+ +	8	6,86	0,19	1	2,14	0,61	9
— —	— —	185	172,36	0,93	41	53,70	3,00	226
		600	76,24%		187	23,76%		787
			$\chi^2_{(8)} = 10,09$				$p = 0,26$	

nach der gleichen Richtung. Bei einer Analyse der Ergebnisse läßt sich zeigen: Von den 9 möglichen Musterkombinationen auf Hypothenar und Thenar beider Hände sind die folgenden bei den Patienten erheblich:

häufiger	dagegen seltener
Hypothenar++Thenar++	Hypothenar——Thenar——
Hypothenar++Thenar+—	Hypothenar+—Thenar——
Hypothenar+—Thenar++	Hypothenar——Thenar+—

während die folgenden Musterkombinationen keinen deutlichen Unterschied zwischen Patienten und Kontrollgruppen erkennen lassen:

Hypothenar++Thenar——
Hypothenar+—Thenar+—
Hypothenar——Thenar++

(Hier sind also Personen und nicht Hände miteinander verglichen worden. Siehe Fußnote Seite 113.)

7. Bemusterung der Hände, Musterzahl pro Hand und Person

Unsere Hand weist, wie aus dem bereits Gesagten und aus den Abbildungen ersichtlich, 5 Musterfelder auf, von denen jedes einzelne 0, 1, 2 oder zuweilen auch 3 Muster aufweisen kann. Es wurde die Gesamtzahl der Muster pro Hand und pro Patient bei den Patienten und bei den Zwillingen verzeichnet und die Zahlen miteinander verglichen. Dieser Vergleich ist bei kurvenmäßiger Darstellung besonders deutlich zum Ausdruck gekommen. Zunächst ist zu sehen, daß bei beiden Populationen sowohl bei Männern wie bei Frauen, die rechten und linken Hände identisch sind (Kurven 1 und 2).

Vergleicht man die Musterzahlen bei ♂♂ und ♀♀ Personen (Kurve 3), so erhält man bei den Patienten – unter Berücksichtigung der kleineren Zahl von ♂♂ ein ziemlich identisches Bild, bei dem bereits die Zweigipfligkeit der Kurve zum Ausdruck kommt. Auch bei den Zwillingen ist ein einwandfreier Unterschied zwischen ♂♂ und ♀♀ nicht nachweisbar. Bei den Zwillingen fehlt aber die Zweigipfligkeit (Kurve 4).

Faßt man ♂♂ + ♀♀, rechts + links zusammen (Kurve 5), so tritt die Zweigipfligkeit der Kurve bei den Patienten noch deutlicher hervor, die dadurch zustande kommt, daß bei den Patienten vom Maximum von 4 Mustern pro Person bis zu 6 Mustern ein Abfall, dann aber bei 7 Mustern pro Person wieder ein Anstieg erfolgt, während bei den normalen Kontrollen vom gleichen Maximum von 4 Mustern pro Person ein gleichmäßiger Abfall vorhanden ist. (Statistisch ließ sich die Bimodalität nicht sichern.)

8. Handfurchung, die 3 Stufen nach Tillner (Abb. 7, 9, 11).

Wir wenden uns nunmehr wieder dem bereits in der Einleitung erwähnten zweiten und gröberen Handliniennetz zu, das neben dem Papillarleisten-

system auf der Hand eingezeichnet ist, nämlich dem Furchensystem. Bei den Handfurchen müssen grundsätzlich zwei verschiedene Typen unterschieden werden, und zwar zunächst die Hauptfurchen oder Primärfurchen. Zu diesen gehören vor allem die den Daumenballen umschließende Daumen-

Tabelle 10

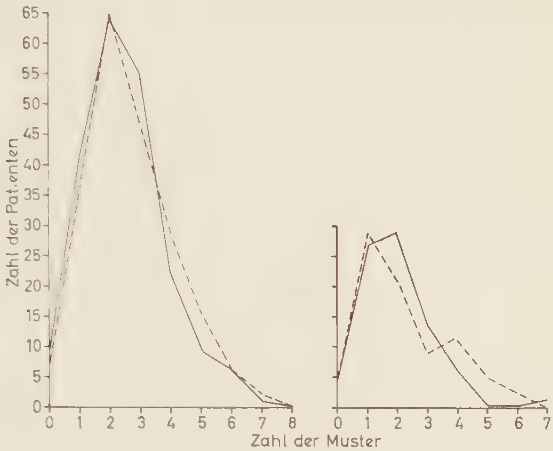
Musterzahl pro Hand und Person

Zahl der Muster	206 ♂ Patienten r	206 ♂ Patienten l	206 ♂ Patienten r+l	82 ♀ Patienten r	82 ♀ Patienten l	82 ♀ Patienten r+l	♂ + ♀ r+l
0	8	6	1	2	4	1	2
1	41	37	6	16	14	3	9
2	64	65	17	30	32	6	23
3	55	46	33	15	14	11	44
4	22	28	33	10	10	19	62
5	9	16	34	8	6	13	47
6	6	6	22	1	2	5	27
7	1	2	27			12	39
8			15			6	21
9			7			4	11
10			2			1	3
11			4			0	4
12			3			1	4
13							
14							

Zwillinge n = 83 Zwillinge n = 104

Zahl der Muster	Hände ♂ r	Hände ♂ l	Person ♂ r+l	Hände ♀ r	Hände ♀ l	Person ♀ r+l	Patient ♂ + ♀ r+l
0	4	4	1	4	6	2	3
1	27	29	6	38	29	4	10
2	29	21	13	38	32	14	27
3	16	9	18	19	20	19	37
4	6	11	12	6	7	27	39
5		5	11	3	3	18	29
6		2	9	2	1	7	16
7	1		4	1	1	9	13
8			6			0	6
9			3			0	3
10						1	1
11						2	2
12						0	0
13						0	0
14						1	1

furche und weiter distal, quer oder schräg verlaufend, die Fünffingerfurche und die Dreifingerfurche. Die übrigen Haupt- oder Primärfurchen der Hand sind Längsfurchen, die als Mittelfingerfurche, Ringfingerfurche und Kleinfingerfurche mehr oder weniger weit distalwärts zu verfolgen sind.



Kurve 1:
Hand, Musterzahl

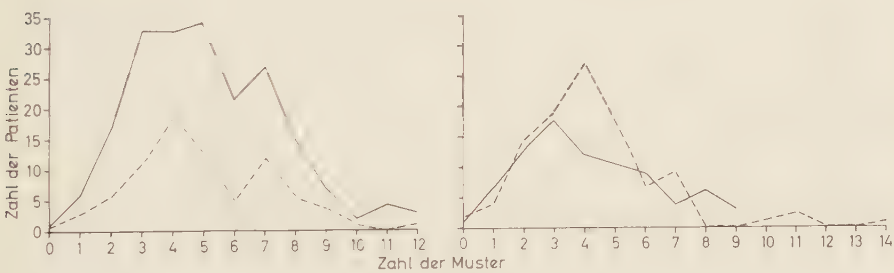
Patienten ♂ ———— r
(200) - - - - - l

Zwillinge ♀ ———— r
(83) - - - - - l

Kurve 2:
Hand, Musterzahl

Patienten ♂ ———— r
(82) - - - - - l

Zwillinge ———— r
(104) - - - - - l



Kurve 3: Hand, Muster pro Person

Patienten ♂ r + l ———— n (206) Zwillinge ♂ r + l ———— n (83)
♀ r + l - - - - - n (82) ♀ r + l - - - - - n (104)

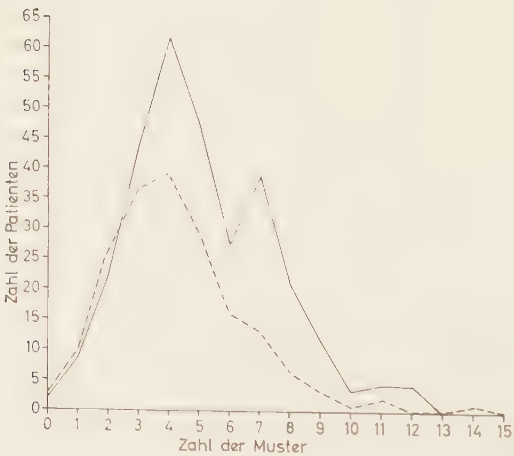
Die bei vielen Menschen sichtbare «M-Figur» wird durch den Schnitt der Mittelfingerfurche mit der Dreifinger- und Fünffingerfurche gebildet. Zu diesen Hauptfurchen gehört, wie in der Einleitung bereits erwähnt, auch die Vierfingerfurche, wenn auch nicht ausschließlich, als pathologische Bildung. Bei unserem Krankengut, bei dem mongoloide Idioten nicht berücksichtigt wurden, war die Vierfingerfurche nicht häufiger als bei den beiden normalen Vergleichspopulationen (Abb. 11, 12).

Der zweite Anteil des Handfurchensystems wird von den Nebenfurchen oder Sekundärfurchen gebildet, auch Querfurchen genannt, die als schräg oder quer verlaufende, unregelmäßige Linien und Falten die Handfläche in sehr verschieden tiefer Ausprägung und Intensität durchziehen können. Die Ausbildung dieser Sekundärfurchen ist – im Gegensatz zum bisher

Kurve 4: Hand, Musterzahl pro Person

♂ r + l
Patienten (206) ————
Zwillinge (83) – – – – –

♀ r + l
Patienten (82) ————
Zwillinge (104) – – – – –



Kurve 5:
Hand, Musterzahl pro Person

♂ + ♀, r + l
Patienten (288) ————
Zwillinge (187) – – – – – –

$10 \cdot 9 \cdot 6 \cdot 5''\text{–}t't''\text{–}S \cdot L_v^c/Q/L^r \cdot 0 \cdot L \cdot D_v$

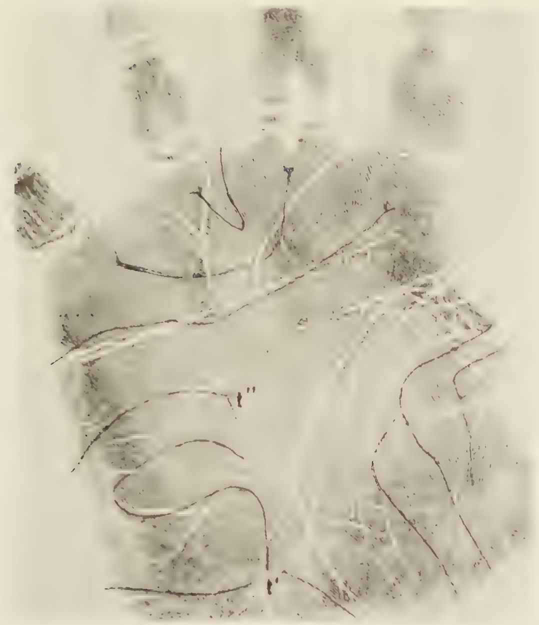


Abb. 9

Musterreichtum auf Thenar und Hypothenar, zwei axiale Triradien. Furchungssystem: Ausgesprochene Sekundärfurchen (Furchungsgrad 3).

betrachteten Papillarleistensystem – mit der Geburt nicht abgeschlossen. Mindestens ein genetischer Faktor für das Furchenbild ist als sicher anzunehmen, doch sind für die Manifestation der sekundären Querfurchen exogene Faktoren bedeutungsvoll. *Wendt* bestätigt auf Grund von sehr detaillierten Untersuchungen an 2000 Personen die erbliche Grundlage für die Handfurchung des Menschen, ebenso wie die Geschlechtsunterschiede und Altersvariabilität. Von exogenen Faktoren erscheint ihm vor allem der alltägliche Handgebrauch für die individuelle Ausprägung des sekundären Handfurchenbildes bedeutungsvoll: Schwere Handarbeit vermindert die Furchendichte, Hausfrauenarbeit vermehrt sie. Allem Anschein nach wirkt die Hornhautbildung bei Handarbeitern der Ausbildung sekundärer Furchen entgegen. *Wendt* glaubt, daß allein aus dem Zusammenwirken von erblicher Grundlage und Umweltfaktoren die Variabilität der Handfurchung erklärt werden kann, fordert aber mit Recht noch gezielte Untersuchungen zur Auffindung weiterer wirksamer Umweltfaktoren.

$11 \cdot 9 \cdot 7 \cdot 5' - 5' \cdot t \; L^{u}_{v} \; T \cdot L^{c} \; L^{r} \cdot D \cdot L \cdot D_{v}$

Abb. 10

Musterreichtum auf Thenar und Hypothenar. *Bettmann*sche Figur (dreifaches Muster auf dem Thenar) und doppeltes Muster auf dem Hypothenar, das obere ohne Triradius t″. Ein axialer Triradius t – Muster in IR II, III und IV: im ganzen acht Muster auf der Hand. Furchungssystem: Sekundäre Furchung mittleren Grades (Furchungsgrad 2).

Nach *Ingo M. Debrunner* sind bei der Geburt die Sekundärfalten einigermaßen gleichmäßig über die ganze Handfläche ausgebreitet, während im Laufe des Lebens die ulnare Region mehr oder weniger frei von sekundären Furchen wird. *Debrunner* hat auch versucht, zwischen der Ausbildung der sekundären Furchen und psychosomatisch pathologischen Befunden bei Anomalen, bei Geisteskranken, aber auch bei überdurchschnittlich Begabten Beziehungen nachzuweisen. *Debrunners* sehr detaillierte Untersuchungen des Handfurchensystems sind von uns nicht angewandt worden. Wir haben uns vielmehr zunächst damit begnügt, nach *Tillner* 3 Stufen des Furchungsgrades zu unterscheiden:

1. Das Furchungsbild beschränkt sich ausschließlich oder fast ausschließlich auf die erwähnten Hauptfurchen, wobei die stets vorhandene Querfurchung am Thenar nicht berücksichtigt wurde (Abb. 7);

2. die sekundäre Handfurchung ist auch in den medialen und distalen Bezirken ausgeprägt, dagegen nicht oder in nur geringem Maße in den ulnaren Handbezirken (Abb. 4);

3. die Sekundärfurchung ist über die gesamte Handfläche ausgebreitet: oft sind die Hauptfurchen kaum sichtbar (Abb. 9).

Ein Unterschied im sekundären Furchenbild zwischen den Patienten und den Zwillingen ist mit einem p 0,32 nicht gesichert. Dagegen besteht eine hohe statistische Sicherung zwischen P und M sowie auch zwischen M und Z (Tab. 11). – Diese Ergebnisse werden nur deshalb erwähnt, weil sich die Patienten von den beiden Normalbevölkerungen in der gleichen Richtung unterscheiden, indem furchenarme Hände (Stufe 1) bei den Patienten seltener, furchenreiche Hände (Stufe 3) dagegen bei den Patienten häufiger sind als bei den beiden Normalbevölkerungen.

Tabelle 11

Die Sekundärfurchung der Hand (drei Stufen des Furchungsgrades)

	Beob.-wert	Erwartungs-wert	χ^2	Beob.-wert	Erwartungs-wert	χ^2	
		Patienten (P)			Zwillinge (Z)		P+Z
Furchungsgrad 1	16	19,24	0,55	16	12,76	0,82	32
Furchungsgrad 2	177	178,59		120	118,41		297
Furchungsgrad 3	86	81,18	0,29	49	53,82	0,43	135
	279	60,13		185	39,87		464
	$\chi^2_{(2)} = 2{,}09$				$p = 0{,}32$		
		Patienten (P)			Marburg (M)		P+M
Furchungsgrad 1	16	46,97	20,45	132	101,02	9,51	148
Furchungsgrad 2	177	172,03		365	369,97		542
Furchungsgrad 3	86	59,99	11,27	103	129,01	5,24	189
	279	31,74		600	68,26		879
	$\chi^2_{(2)} = 46{,}47$				$p < 10^{-10}$		
		Marburg (M)			Zwillinge (Z)		M+Z
Furchungsgrad 1	132	113,12	3,1	16	34,88	10,22	148
Furchungsgrad 2	365	355,40	0	120	114,31	0	485
Furchungsgrad 3	103	116,17	1,49	49	35,83	4,13	152
	600	76,43		185	23,57		785
	$\chi^2_{(2)} = 18{,}99$				$p = 0{,}0001$		

$9 \cdot 7 \cdot 5'' \cdot 4\text{–}tt^{u}\text{–}L_{u}^{v} \cdot 0 \cdot 0 \cdot 0 \cdot L/D_{v}$

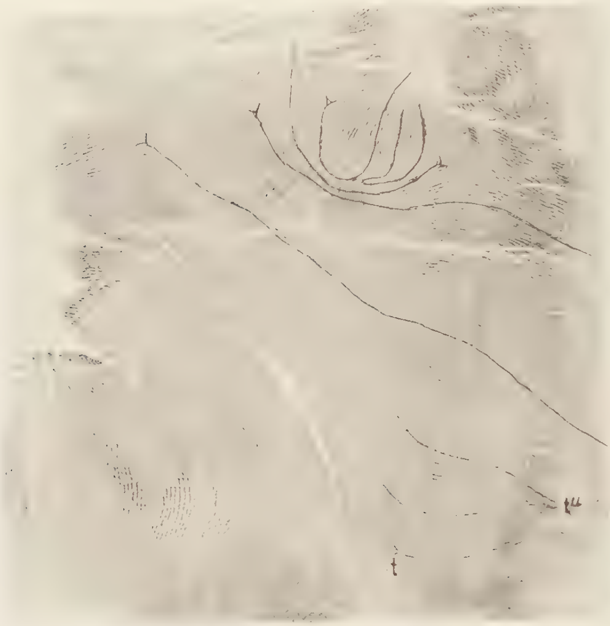


Abb. 11

Vierfingerfurche (Sperrfurche, Affenfurche) teilt die Hand in einen distalen und einen proximalen Abschnitt. Spurenmuster am Hypothenar, zwei axiale Triradien. Sekundäres Furchungssystem mittleren Grades (Furchungsgrad 2). (Rechte Hand).

Diskussion der Ergebnisse

Angesichts unserer Hauptergebnisse, des größeren Musterreichtums der Palma bei cerebral anomalen und in der geistigen Entwicklung zurückgebliebenen Kindern im Vergleich zu 2 Normalpopulationen, stellt sich zunächst die Frage, was über Musterzahl und Musterverteilung im Vergleich zu den musterfreien Feldern der menschlichen Hand bei den verschiedenen Völkern und ethnischen Gruppen bekannt ist. Die Schwankungen sind in der Tat beträchtlich, und auffallenderweise ist bei den wichtigsten ethnischen Gruppen der Welt die Musterhäufigkeit in den einzelnen Handbezirken unterschiedlich verteilt. Selbstverständlich handelt es sich hier lediglich um Unterschiede in der Verteilung der gleichen Musterformen bei verschiedenen Populationen. Im Einzelfall kann aus der Musterverteilung nicht etwa auf die Zugehörigkeit zu der oder jener ethnischen Gruppe oder

9·7·5'·4–t–L^{r}–0–m–0–L/D$_{v}$

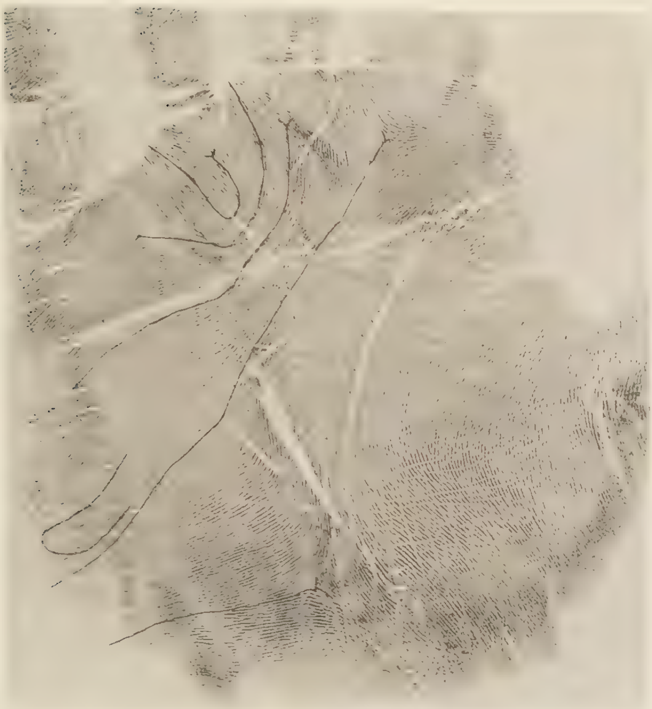


Abb. 12

Linke Hand des gleichen Patienten. Vierfingerfurche, Schleifenmuster auf dem Hypothenar und in IR IV, ein axialer Triradius. Sekundärfurchung mittleren Grades (Furchungsgrad 2).

Population geschlossen werden. Eine gute Übersicht gibt eine nach *Rife* (1954) zusammengestellte Tabelle der prozentualen Musterhäufigkeit der verschiedenen Handregionen (pro Hand):

	Thenar	Hypothenar	IR II	IR III	IR IV
Westeuropäer	10 (15–20)	35	5	40	60
Europ. Amerikaner	12 (15–20)	37	12	–	60
Mittlerer Osten	15	40	8	55	55
Mongolen	8	15	3	20	75
Indianer	35	15	3	30	70
Neger	15	18	15	35	85

Bei der Analyse dieser Tabelle kann man die quantitativen Unterschiede der Leistenmuster wie folgt zusammenfassen:

Am *Thenar* haben die Westeuropäer (und Mongolen) die niedrigsten, Indianer die höchsten Werte;

am *Hypothenar* fallen die hohen Werte der 3 ersten Gruppen im Vergleich u den übrigen auf;

im *IR II* sind die hohen Werte bei Negern (und europäischen Amerikanern) im Vergleich zu den übrigen Gruppen auffallend;

im *IR III* stehen Mittlerer Osten, dann Westeuropäer an der Spitze;

im *IR IV* haben die Neger die höchsten Werte, doch sind die Werte bei allen Populationen hoch.

Jede dieser ethnischen Gruppen unterscheidet sich also von jeder andern durch deutliche Variationen auf einem oder auf mehreren Handbezirken. Wenn wir die gleiche prozentuale Berechnung der Musterhäufigkeit pro Hand bei unseren beiden Normalpopulationen Z und M und bei den Patienten (P) vornehmen, so ergibt sich zum Vergleich die folgende Tabelle:

	Thenar	Hypothenar	IR II	IR III	IR IV
Z	16,31	54,54	6,68	39,04	64,17
M	13,00	48,17	5,50	42,00	61,42
P	28,55	71,28	10,38	45,67	60,55

Der Vergleich lehrt zunächst, daß unsere beiden Normalbevölkerungen Z und M im Vergleich zu den im Schrifttum anerkannten Zahlen vor allem am Hypothenar ungewöhnlich musterreich sind, daß auch am Thenar verhältnismäßig hohe Werte erreicht werden, während IR II, IR III, IR IV im Bereich des üblichen liegen. Hierbei kann auch eine unterschiedliche Bewertung vorhanden sein: es ist sehr wohl denkbar, daß trotz der allgemein anerkannten und angestrebten internationalen Nomenklatur (*Cummins, Keith, Midlo, Montgomery, Wilder* und *Wipple Wilder*) die einzelnen Untersucher sich in der Bewertung und Bezeichnung zum Beispiel von Spurenmustern (V) oder kleinen Schleifen voneinander unterscheiden. Es ist daher wichtig, daß bei unseren Untersuchungen nicht nur die vorliegenden statistischen Werte berücksichtigt, sondern daß 2 Normalpopulationen zum Vergleich herangezogen worden sind, die von den gleichen Untersuchern nach genau den gleichen Grundsätzen und der gleichen «Musterbewertung» untersucht wurden.

Die Werte bei unseren Patienten unterscheiden sich von den oben verzeichneten 6 ethnischen Gruppen durch ihren ungleich größeren Musterreichtum.

Eine Bemusterung von 71% auf dem Hypothenar ist bei keiner einzigen der ethnischen Gruppen auch nur im entferntesten erreicht, und die Be-

musterung von 28% auf dem Thenar ist ausschließlich bei den Indianern mit 35% übertroffen.

Bevor wir unsere Ergebnisse weiter analysieren können, muß auf die gegenwärtigen Anschauungen über die *Bedeutung von Erbe und Umwelt* für die Bildung der Handmuster eingegangen werden. Da die Dermatoglyphen in der ersten Hälfte der fötalen Entwicklung geformt und gebildet werden, sind sie von postnatalen Faktoren unbeeinflußt. Korrelationen zwischen den Leistenmustern und anderen Eigenschaften haben daher mit postnatalen Bedingungen nichts zu tun. Gerade auf Grund dieser ziemlich einzigartigen Eigenschaften besitzen die Dermatoglyphen große Möglichkeiten der Verwertung in der menschlichen Biologie, die bisher noch nicht genügend ausgenutzt worden sind.

Auch in der Tabelle von *Baitsch und Bauer*, in der unter anderem die Hypothenarbemusterung in 57 Normalpopulationen der Welt verzeichnet ist, werden die Prozentzahlen unserer Patienten (71% Muster auf dem Hypothenar, 28% Muster auf dem Thenar) nicht erreicht. Bei 14 in dieser Tabelle zusammengestellten deutschen Populationen schwankt die Bemusterung des Hypothenar zwischen 29,8 und 50,4 mit einem Durchschnitt von 38,74. Bei den 43 nicht deutschen Gruppen ist der Durchschnitt 17,84. Am Thenar ist der Durchschnitt der 14 deutschen Gruppen 15,0 (2,6–29,1), der 43 nicht deutschen Gruppen 15,56.

Einige Autoren *(Weninger, Becker und Meißner, Rife)* diskutierten die Möglichkeit monomerer *Erbgänge*, ohne jedoch zu einem der Kritik standhaltenden Ergebnis zu gelangen. In Wirklichkeit dürfte eine sehr komplizierte multifaktorielle Vererbung vorliegen, wobei manche Gene nur einzelne Bereiche, manche Gene aber mehrere betreffen dürften, da Korrelationen zwischen den einzelnen vorkommen (Pleiotropie). Auch *Rife* ist bei seinen Untersuchungen zu dem Schluß gekommen, daß die vorwiegend quantitativen Veränderungen auf multiplen Genen beruhen, durch die in der Hand Mustertyp und Musterhäufigkeit in den 5 palmaren Regionen bestimmt werden.

Es scheint im übrigen sicher zu sein, daß für die Handmuster erbliche Faktoren eine geringere Rolle spielen als etwa an den Fingerbeeren Leistenanzahl und Fingermuster.

Interessant sind in diesem Zusammenhang die Untersuchungen von *Degenhardt und Geipel* über das Tastleistensystem bei phokomelen Entwicklungsstörungen. Hier waren die Ausfälle und Anomalien im Hautleistensystem der Palma viel tiefgreifender als die der später entstehenden Fingerleisten. Diese Tatsache beweist, daß die Entwicklungsstörungen im allerfrühsten Embryonalstadium gewirkt haben. Die Musterformen, die bei

diesen Entwicklungsstörungen vorlagen, führten zu dem Schluß, daß die Leistenbilder ein zum Teil passiver Vorgang sind, der zum großen Teil durch die unmittelbare Umgebung bedingt ist. – In Analogie hierzu kann man vermuten, daß diejenigen Faktoren, die bei unseren Patienten zu der ungewöhnlich starken palmaren Musterbildung geführt haben, im allerfrühesten Embryonalstadium eingewirkt haben, wobei es offenbleiben muß, ob diese Faktoren genetischer oder nicht genetischer Natur waren.

Zugleich wird auch verständlich, daß sich eine Beziehung zwischen *Finger*leistenmuster und cerebralen Störungen nicht hat nachweisen lassen (siehe zweiter Teil unserer Arbeit, vor allem Seite 189): Zur Zeit der Entstehung der *Finger*leisten (3.–5. Embryonalmonat) war allem Anschein nach die Wirkung derjenigen Faktoren bereits abgeschlossen, die zu einem früheren embryonalen Zeitpunkt (vor dem 3. Embryonalmonat) sowohl auf die Ausbildung von *Hand*leistenmustern, als auch auf die cerebrale Entwicklung eingewirkt haben. Zu dieser Annahme paßt auch die Tatsache, daß bei vielen durch Erbe und Umwelt – oder beides – bedingten cerebralen Störungen für die Entstehung eine solche sehr frühe embryonale Epoche nachgewiesen werden konnte.

Der *Grundplan der Primatenhand* (Abb. 1) zeigt die Ballen des Thenar, Hypothenar, der IR I, II, III, IV, außerdem II^r radialwärts von IR II und IV^u ulnarwärts von IR IV. Alle diese Ballen – einschließlich II^r und IV^u – sind auch beim menschlichen Fötus zu finden. Diese Ballenbezirke der frühen Fötalzeit bilden sich beim menschlichen Fötus später zurück. In sämtlichen dieser 9 Ballenbezirke sind Wirbel oder Schleifen als Muster eingezeichnet, außerdem eine Reihe von achsialen und ulnaren Triradien. In der Tat besteht zwischen *Ballen und Leistenbildung* eine enge Beziehung, indem allem Anschein nach beide durch die gleichen Wachstumsfaktoren der Fötalzeit bedingt werden.

In der Evolution ist der Ballen mit einem Wirbel verbunden. Man kann daher annehmen, daß der *Wirbel das primitivste Muster* darstellt und daß die anderen Muster fortgeschrittene Bildungen sind. Je mehr die Muster der Handfläche dem Grundplan entsprechen, umso primitiver, je mehr sie von dem Grundplan abweichen, desto spezialisierter ist der Zustand. Wirbel und wirbelartige Muster sind also primitiv, weniger komplizierte Muster oder musterfreie Felder weisen auf einen fortgeschrittenen Zustand (etwa auf eine Wendung vom Schreiten zum Greifen), bilaterale Symmetrie ist primitiv, Rechts-Links-Unterschiede treten im Zuge der Spezialisierung auf.

Interessanterweise geht bei der Anlage und beim Verschwinden der Ballen und beim Bauplan der Leisten die fötale menschliche Entwicklung

mit der phylogenetischen Geschichte weitgehend parallel. (Hier scheint also das «biogenetische Grundgesetz» von *Häckel* zu gelten).

Nach *Bonnevie* wirken die Dicke und die wohl vom Flüssigkeitsgehalt abhängige zeitweilige Polsterung der fötalen Epidermis zur Zeit der Musterbildung sowie Variationen der fötalen Ballenrückbildung auf die Leistenausbildung, indem um so weniger Wirbel und Schleifen entstehen, je stärker diese Polsterung und je dicker die fötale allgemeine Epidermis war. Auf der anderen Seite besteht eine Beziehung zwischen der Zeit der Ballenrückbildung und der Leistenausbildung in dem Sinne, daß um so weniger Muster auftreten, je früher die Rückbildung erfolgt. Wo sich, wie am Thenar, die Ballen in der frühen Fötalzeit zurückbilden, sind die Bezirke oft frei von Mustern. Wo sich, wie in den distalen Phalangen, die Ballen länger halten, haben wir häufig hochentwickelte Muster.

Wenn wir unsere Ergebnisse im Lichte dieser Tatsachen betrachten, so muß allerdings vorausgeschickt werden, daß es sich auch um eine zufällige Parallelität handeln kann, die über phylogenetische Beziehungen nichts auszusagen braucht.

Immerhin kann kein Zweifel darüber bestehen, daß die Tastleisten in den Händen unserer Patienten dem eben besprochenen Grundplan der Primathand erheblich ähnlicher sind als bei den beiden Normalpopulationen und auch weit ähnlicher als bei anderen veröffentlichten Bevölkerungsgruppen. Sowohl der Musterreichtum wie die Mustervielfältigkeit und die zahlreichen achsialen Triradien betonen den primitiven Zustand. Dieser Eindruck wird noch dadurch verstärkt, daß, wie die Tabellen zeigen, eine bilaterale Symmetrie und ein weniger ausgesprochener Unterschied zwischen ♂ und ♀ Händen ebenfalls auf den primitiven Zustand hinzuweisen scheinen. Wenn man weiterhin die Ergebnisse von *Bonnevie* über Dicke, Polsterung und Ballenrückbildung der fötalen Epidermis auf unsere Ergebnisse anzuwenden versucht, so würde der größere Musterreichtum der Patienten dafür sprechen, daß bei ihnen die fötale Epidermis dünn gewesen ist, ein Befund, der bereits in einer früheren Publikation *(Geipel und Hirsch)* im Zusammenhang mit dem größeren Wirbelreichtum cerebral geschädigter Kinder ausgesprochen worden ist. – Weiterhin kann der größere Musterreichtum dafür sprechen, daß die fötale Ballenrückbildung verzögert oder verspätet eingetreten ist.

Für eine Verbindung zwischen Tastleisten- und Zentralnervensystem spricht die Tatsache, daß Haut- und Nervensystem ektodermale Gewebe sind, und daß die für die Funktion der Dermatoglyphen entscheidenden sensiblen Nervenenden im Grunde der Tastleisten münden: Auf Grund anatomisch-embryologischer Untersuchungen *Bonnevies* kann die Frage

diskutiert werden, ob die Papillarleistenbildung von den Nerven ursächlich ausgelöst wird oder ob Tastleistenbildung und Nervenwachstum Ausdruck eines übergeordneten Prinzips sind.

Die großen Unterschiede im Tastleistensystem der Hand zwischen normalen Personen und cerebral geschädigten Kindern berechtigen zu der Frage, ob die *Analyse des Handabdruckes als klinisch-diagnostische Methode* eingeführt werden sollte, das heißt, ob auch im klinischen Einzelfall – und nicht nur in der Gruppe – Unterschiede zwischen normalen und cerebral geschädigten Menschen zu erwarten sind. Unsere Untersuchungen (siehe vor allem unter 6 und 7) sprechen dafür.

Es bleibt zu untersuchen, ob diese Patienten mit einem besonderen Musterreichtum beider Hände auch klinisch einer besonderen Gruppe entsprechen, die zu einer weiteren «Unterteilung des buntgewürfelten Syndroms oder sogar nur Symptoms der Oligophrenie» *(Richterich)* führen könnte. Ein Ergebnis solcher Untersuchungen sollte erstrebt werden.

Zusammenfassung

1. Im Rahmen von genetisch-klinischen Untersuchungen an cerebral geschädigten und in ihrer geistigen Entwicklung zurückgebliebenen Kindern wurde das Papillarleisten- und Furchenbild der Handfläche bei 289 anomalen Kindern untersucht, die im «Kindersanatorium Wiesengrund», einem zum Bezirksamt Reinickendorf des Senats von Berlin gehörenden Kinderheim, auf der klinischen und pädagogischen Station waren.

2. Von diesen 289 anomalen Kindern waren 207 männlich, 82 weiblich. Es ließ sich zeigen, daß bei unserem Krankengut das männliche Geschlecht um das 2½fache häufiger von cerebralen Schäden betroffen war als das weibliche.

3. Bei allen Kindern konnte eine angeborene, genetisch oder frühfötal bedingte Anlage für ihre abwegige psychische und intellektuelle Entwicklung angenommen werden.

4. Zur Kontrolle dienten 2 Normalpopulationen, 187 Berliner Zwillinge (83 ♂♂, 104 ♀♀) und 600 normale Personen (300 ♂♂, 300 ♀♀) einer von *G.G. Wendt* (Marburg/Lahn) zusammengestellten gemischten Population.

5. Am *Hypothenar* hatten die Patienten eine weit stärkere, statistisch hoch gesicherte Bemusterung, die einfache wie zusammengesetzte Muster und eine größere Variation in der Ausgestaltung der zusammengesetzten Muster betrafen.

6. Auch auf dem *Thenar* ist die weitaus größere Musterhäufigkeit bei

den Patienten statistisch hoch gesichert. Die Unterschiede betreffen vor allem einfache Muster und sichere Spuren.

7. Bei 195 Patienten-*Eltern und Geschwistern* zeigte sich, daß diese in bezug auf ihre *Hypothenar*-Bemusterung in der Mitte zwischen Patienten und Normalpersonen standen: Sie hatten weniger Muster als die Patienten, aber mehr als die Kontrollpersonen. In bezug auf die *Thenar*bemusterung sind dagegen Patienten und Familien identisch. – Diese Ergebnisse werden dadurch verständlich, daß sich unter den Eltern und Geschwistern der Patienten eine nicht geringe Zahl von cerebral abwegigen Personen befanden. Auf die Unterschiede *zwischen den beiden Normalbevölkerungen* sei besonders hingewiesen. Diese Unterschiede ändern an der Bedeutung unserer Ergebnisse deshalb nichts, weil sich beide Normalpopulationen in der gleichen Richtung von den Patienten unterscheiden.

8. Bei den *achsialen Triradien* haben die Patienten mehr Kombinationstypen. Außerdem ist die Zahl der Patienten mit 2,3 oder mehr Triradien ganz erheblich größer als die der Normalpersonen. Die Unterschiede sind statistisch hoch gesichert.

9. In den Interdigitalräumen II und III ist eine Tendenz zu häufigerer Bemusterung und daher seltener Ausbildung freier Felder bei den Patienten zu verzeichnen. Diese Unterschiede sind aber nicht immer statistisch gesichert.

10. Im Interdigitalraum IV sowie in den Hauptlinienendigungskombinationen unterscheiden sich die Patienten nicht von den beiden Normalpopulationen.

11. Kombinationen von Thenar- und Hypothenarmustern

Von den 9 möglichen Musterkombinationen auf Hypothenar und Thenar beider Hände überwiegen bei den Patienten die Fälle, wo von den 4 Regionen (2 Hypothenare und 2 Thenare der beiden Hände des Patienten) alle 4 oder 3 bemustert sind. Dagegen kommt es bei den Patienten seltener vor, daß keine oder nur eine Region bemustert ist. Die Unterschiede sind statistisch sehr hoch gesichert.

12. Zeichnet man die *Gesamtmusterzahl pro Hand und pro Person* als Kurve, so weist diese nur bei den Patienten eine Zweigipfligkeit auf, wobei das zweite Maximum bei 7 Mustern pro Person gelegen ist. Schon daraus ist auf multifaktorielle Ursachen zu schließen.

13. Es besteht bei den Patienten eine Neigung zu stärkerer Ausprägung des *sekundären Furchensystems;* diese Unterschiede sind aber statistisch nicht gesichert.

14. Unsere Patienten unterscheiden sich auch von den im Schrifttum

angegebenen *ethnischen Gruppen* durch ihren ungleich *größeren Musterreichtum.*

15. Die Faktoren, die zu der ungewöhnlich starken Musterbildung führen, haben vermutlich im allerfrühsten Embryonalstadium eingewirkt *(Degenhardt und Geipel)*.

16. Mit aller Vorsicht im Urteil wird festgestellt, daß die Musterausbildung unserer Patienten dem Grundplan der Primatenhand ähnlich ist und also – im Sinne der *Evolution* – einen *primitiven Zustand* darstellt. Im Lichte der Arbeiten von *Bonnevie* ist bei den Patienten eine dünne fötale Epidermis anzunehmen, und die fötale Ballenrückbildung könnte bei ihnen verspätet eingetreten sein.

Summary

Palmar dermatoglyphics have not been systematically examined in patients presenting signs of abnormal cerebral development or cerebral damage apart from Mongolism. The present authors have previously shown in a group of children suffering from neurotic maldevelopment of their personality that the number of individuals showing no C main line was significantly increased and that small transversal and oblique "secondary" creases were more common in this group than in normals.

In the present investigation the palmar dermatoglyphics of 289 mentally abnormal children (207 males, 82 females) have been compared with those of two control groups: 1. 187 Berlin twins (83 males, 104 females) and 2. 600 healthy persons (300 males, 300 females) from various parts of the Western German Republic.

The sex-ratio among the patients was thus greatly increased. In 38 families with two or more children presenting cerebral damage this ratio was 2.5:1 whereas in the total of 224 families of the patients no sex difference could be shown between the normal children (139 males : 151 females).

In all the patients the psychological and intellectual maldevelopment could be assumed to be due either to hereditary factors or disturbances in early foetal development. The main findings were as follows:

1. *Hypothenar.* In interpreting the hypothenar patterns a distinction was made between two types: a) single or primary patterns, and b) combined or complex patterns, i.e. pattern within pattern, duplex or triplex hypothenar configurations etc. – More variations of combined patterns were found in the patients resulting in a more complex and "coloured" picture. True hypothenar patterns were much more frequent in the patients,

the difference being highly significant. The well-known correlation between the two hands would, however, lead to an overestimation of the significance, but a comparison of persons for patterns and open fields was also highly significant. In contrast with the findings in the normal groups the patients presented no sex difference in regard to the number of hypothenar patterns. Both normal groups differed from the patients in the same direction as both had less patterns and more open fields than the patients. Hypothenar pattern and open field distribution in 195 parents and sibs of the patients showed these to be placed between the patients (P) and the normal groups (Z and M). The difference was significant between the families and the Z or M group, even if much less than the difference between P and Z or M. These results were in accordance with expectation as 38 families included more than one mentally abnormal child and in at least 45 other families the mothers were not normal.

2. *Thenar.* In the interpretation of thenar and first interdigital dermatoglyphics together, single patterns, vestiges and composed patterns (*Bettmann* configuration) have been compared with open fields. Patterns occurred more often among the patients than in the two normal populations. As in the hypothenar also in the thenar Z and M differed from P in the same direction, hereby substantiating the pattern difference found to exist between abnormal and normal individuals. This higher number of thenar patterns in the patients concerned single patterns and vestiges only, whereas the *Bettmann* configuration seemed to be equal in the three populations.

3. *Axial triradii.* Comparing the three populations as to the number, types and combinations of axial triradii the patients showed 32 different types, Z 22, M 26. This richer and more "coloured" picture was present in those hands only which had three or more combinations, P showing 17, Z 8 and M 9 different combinations with preponderance of females. With all three populations behaving in the same way we would have had to expect less different combinations of triradii in our patients. The fact that there were more types in the P group in spite of the lower number of females strengthens our results. The number of hands showing 1, 2 or 3 and more triradii (independent of combination types) in the three groups were compared. The two normal groups were found to be identical, both differing from the patients in the same direction, i.e. persons with 2, 3 or more triradii occurred much more often in the group of patients.

4. *Second, third and fourth interdigital areas.* Statistically it was only possible to compare the number of patterns with open fields in each area. In these areas, however, rather wide variations seemed to occur between

right and left, male and female, in all three populations. These normal variations made the value of a statistical estimate doubtful. Besides this, the differences were far from being impressive.

5. *Main lines (modal types), tracing and terminal relations.* The 4 main lines A, B, C and D have been traced and classified and the terminal relations have been compared. The patients showed in the B main line more terminal 7 and less terminal 5; and in the D main line more terminal 10 and 8. For main lines A and C no significant differences could be shown for P compared with Z and M. As in the interdigital areas, variations between the normal groups are very wide. A conclusion concerning the degree of transversality of ridges in P as compared with Z and M is not possible. The main line index *(Cummins)*, a record of the termination of lines D and A, as combined in individual palms, was for P 8.52, for Z 8.18 and for M 8.37. The difference is, of course, not significant.

6. *Hypothenar and thenar patterns per person.* As every person has 2 hypothenars and 2 thenars each of which may have patterns or open fields 9 possible combinations have to be considered. Recording these combinations for every *person* in the 3 populations and comparing each combination between P, Z and M, the two normal groups proved to be identical, whereas there was a highly significant difference of P against Z and of P against M.

7. *Total palm patterns, number of patterns per hand and per person.* The total number of patterns per hand and per person was recorded in P and Z and the figures plotted in curves for comparison. The curves of the patients had a double peak (per hand as well as per person, males and females alike), the first for 4 patterns, the second for 7 patterns, whereas Z had one peak only for 4 patterns. Statistically, no bimodality could be ascertained.

8. *Palm creases.* Independent of the palmar dermatoglyphics, a second system of "hand lines" comprises the palm creases, the field of the palmist. Besides the fairly constant major flexion creases, a number of secondary, smaller, transversal or oblique, irregular creases is present, more or less marked in intensity and extension. According to the distribution and amount of secondary palm creases, 3 grades have been distinguished (after *Tillner*): 1. only major flexion creases are present, 2. secondary creases are pronounced in the central and distal areas of the palm, but not in the hypothenar, 3. secondary creases are spread over the whole palm, sometimes even hiding the major flexion creases. – The differences of P against Z or M are not significant. Still, Z as well as M deviate from P in the same direction, and a certain tendency seems to indicate that P had less grade 1 and more grade 3 than Z and M.

9. *Palm dermatoglyphics in German and non-German ethnic groups.* The most important results of our examination may be summarized in the high pattern – percentage of the palm, especially of hypothenar and thenar, in our mentally abnormal and retarded children as compared with two normal populations. The high percentage of hypothenar and thenar patterns in our patients is rather unique; nothing comparable has been found in any of the 65 populations studied previously; only in American Indians the percentage of thenar patterns is higher.

10. *Comparative and embryological considerations.* The basic morphological plan of volar pads and of configurational areas in the palm is apparent in all primates. The palms of our patients were more similar to this "basic" plan than the palms of the two normal groups Z and M and other populations studied so far. High pattern percentage, multipicity and variety in pattern formation as well as the numerous axial triradii emphasized the primitive state. Bilateral symmetry and less outspoken differences between right and left hands may also allude to a more primitive state. According to *Bonnevie* larger pattern variety would mean that a thin foetal epidermis had been present and that the involution of foetal pads had been retarded and delayed.

Résumé

Les dermatoglyphes de la paume ont été longuement étudiés chez les mongoliens. L'existence d'anomalies quasi spécifiques a été rapidement reconnue. Par contre les autres anomalies cérébrales n'ont pas fait l'objet d'études aussi poussées.

Le présent travail compare les dermatoglyphes palmaires de 289 enfants mentalement anormaux (207 garçons, 82 filles) et ceux de deux populations témoins: 187 jumeaux berlinois (83 garçons et 104 filles) et 600 personnes (300 de chaque sexe) provenant des différentes régions de l'Allemagne fédérale. On voit que l'index de masculinité est très augmenté dans le groupe de malades. On retrouve le même déséquilibre dans leurs familles, quand elles contiennent deux ou plusieurs enfants anormaux (38 familles). Si le sujet étudié représente le seul malade (224 familles), la répartition des sexes est égale dans la fratrie saine (139–151).

Chez tous les malades la cause du mauvais développement psychique ou intellectuel peut être rattachée à des facteurs héréditaires ou des anomalies du développement survenues dans les premiers temps de la vie fœtale.

Résultats

1° Sur l'*éminence hypothénar*, on observe chez les malades, par rapport aux témoins, un nombre bien plus élevé de figures simples (boucles, arcs, ébauches de figures) et de figures complexes. La variété de celles-ci est beaucoup plus grande. Les différences trouvées sont statistiquement très significatives.

Ces résultats sont obtenus en comparant dans les deux groupes les mains homonymes chez des sujets de même sexe. Il apparaît en outre que la différence entre les sexes, nette chez les témoins disparaît chez les malades.

La fréquence des figures hypothénariennes chez les parents, frères et sœurs de malades, classe ces sujets dans une zone intermédiaire entre les témoins et les malades. Ceci s'explique par le fait que dans 83 familles, il y avait, outre l'enfant étudié, au moins un autre sujet anormal.

2° *Eminence thénar et premier espace interdigital.* La fréquence des figures simples et des ébauches de figures est également plus grande (différence hautement significative) mais les figures complexes ne sont pas plus fréquentes que chez les témoins. Les familles étudiées ne diffèrent pas ici des sujets normaux.

3° *Combinaison des figures thénariennes et hypothénariennes.* 9 combinaisons sont possibles pour les 2 éminences thénar et les 2 éminences hypothénar de chaque sujet selon qu'elles portent ou non les figures étudiées. Il est habituel chez les malades de trouver trois ou quatre éminences garnies. Les différences sont très significatives d'avec le groupe témoin.

4° *Position des triradius axiaux.* Le nombre de triradius est beaucoup plus élevé chez les malades. Le nombre de combinaisons possibles entre les triradius multiples est également beaucoup plus grand. Le fait qu'il n'y ait pas de sujets féminins parmi les malades augmente encore la valeur de ce résultat.

5° *Les espaces interdigitaux n° 2 et 3* contiennent plus de pelotes chez les malades mais la différence n'est pas statistiquement significative.

6° En ce qui concerne *le quatrième espace interdigital* et la *transversalité des plis de la paume*, les malades ne diffèrent pas des témoins.

7° Si l'on dresse les courbes rassemblant le *nombre total des figures par personne et par main*, pour les malades et les témoins, on trouve:

– chez les témoins, un seul sommet indiquant un maximum à 4 figures.
– chez les malades 2 sommets à 4 et à 7 figures par personne, ce qui suggère l'intervention de plusieurs facteurs déterminants.

8° Indépendamment du système de référence précédent, il existe sur la

paume des plis de flexion principaux (dont l'anomalie la plus grande est le pli palmaire transverse) et des *plis secondaires* divisés en trois degrès par *Tillner*. Il semble exister dans le groupe des malades une certaine tendance, là aussi à la complexité.

9° Les caractères qui opposent les malades aux témoins de race allemande les opposent de la même façon aux divers groupes ethniques dont les dermatoglyphes sont décrits dans la littérature.

10° *Embryologie et anatomie comparée.* Les mains des malades diffèrent des mains de l'homme normal mais se rapprochent d'autres mains de primates. La fréquence des figures, leur complexité, leur variété, le nombre de triradius axiaux, la symétrie des deux mains, rappellent, sous l'angle évolutionniste, les stades primitifs du développement des primates.

Enfin si l'on en croit les travaux de *Bonnevie*, il faut admettre que les malades ont gardé une structure épidermique de type fœtal primitif et que l'involution habituelle des formations palmaires a été entravée.

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Tab. 1: Grundliste Seiten 151 bis 182.

Patienten (207 ♂♂ + 82 ♀♀)

Hypothenar ♂♂

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		207	207	414	207	207	414	207	207	414
V		–	–	–	4	5	9	4	5	9
	%						2,17			2,17
A^r		8	1	9	–	–	–	8	1	9
	%			2,17						2,17
T^r		2	5	7	–	–	–	2	5	7
	%			1,69						1,69
L^r		47	62	109	7	9	16	54	71	125
	%			26,33			3,86			30,19
L^u		10	13	23	20	23	43	30	36	66
	%			5,55			10,39			15,94
L^c		5	2	7	2	–	2	7	2	9
	%			1,69			0,48			2,17
W		8	7	15	–	–	–	8	7	15,
	%			3,62						3,62
S		3	2	5	–	–	–	3	2	5
	%			1,21						1,21
8 einfache Muster			%	42,26			16,90			59,16
A^r/L^r L^r/A^r		7	2	9	–	–	–	7	2	9
	%			2,17						2,17
L^r/L^r		4	2 2	6	–	–	–	4	2	6
	%			1,45						1,45
l_v^r/L^r		2	–	2	–	–	–	2	–	2
	%			0,48						0.48
L_v^u/L^r		2	3	5	1	1	2	3	4	7
	%			1,21			0,48			1,69
L^u/L^u		1	1	2	–	–	–	1	1	2
	%			0,48						0,48
L_v^u/L^u		5	3	8	1	–	1	6	3	9
	%			1,93			0,24			2,17
L^u/T^r		1	–	1	–	–	–	1	–	1
	%			0,24						0,24
L^u/L^c		1	–	1	–	–	–	1	–	1
	%			0,24						0,24
W/l^r		1	–	1	–	–	–	1	–	1
	%			0,24						0,24
l^r/W		1	–	1	–	–	–	1	–	1
	%			0,24						0,24
L^r/T^r		–	1	1	–	–	–	–	1	1
	%			0,24						0,24
$L^u/T^u/T^r$		–	1	1	–	–	–	–	1	1
	%			0,24						0,24

	Muster			Spuren			Gesamt		
	r	l	r+l	r	l	r+l	r	l	r+l
	207	207	414	207	207	414	207	207	414
L^r/L^u	–	1	1	–	–	–	–	1	1
%			0,24						0,24
L^r/L^c	1	1	2	–	–	–	1	1	2
%			0,48						0,48
$L^u_v/L^u/L^r$	–	1	1	–	–	–	–	1	1
%			0,24						0,24
L^u_v/W	–	1	1	–	–	–	–	1	1
%			0,24						0,24
W_v/L^u_v	–	–	–	–	1	1	–	1	1
%						0,24			0,24
$\left.\begin{matrix}L^r/V\\V/L^r\end{matrix}\right\}$	1	1	2	–	–	–	1	1	2
%			0,48						0,48
L^r/l^m	1	–	1	–	–	–	1	–	1
%			0,24						0,24
21 zusammenges. Muster %			11,08			0,96			12,04
29	111	110	221	35	39	74	146	149	295
%	53,62	53,14	53,38	16,91	18,84	17,87	70,53	71,98	71,26

Patienten (207 ♂♂ + 82 ♀♀)

Hypothenar ♀♀

		Muster			Spuren			Gesamt		
		r 82	l 82	r+l 164	r 82	l 82	r+l 164	r 82	l 82	r+l 164
V		–	–	—	2	2	4	2	2	4
	%						2,44			2,44
A^r		1	1	2	–	–	–	1	1	2
	%			1,22						1,22
T^r		2	–	2	–	–	–	2	–	2
	%			1,22						1,22
L^r		16	31	47	3	4	7	19	35	54
	%			28,66			4,27			32,93
L^u		5	4	9	11	5	16	16	9	25
	%			5,49			9,76			15,25
L^c		3	1	4	–	–	–	3	1	4
	%			2,44						2,44
W		5	4	9	–	–	–	5	4	9
	%			5,49						5,49
S		–	–	–	–	–	–	–	–	–
	%									
7 einfache Muster	%			44,52			16,47			60,99
A^r/L^r L^r/A^r		3	1	4	–	–	–	3	1	4
	%			2,44						2,44
L^r/L^r		1	–	1	–	–	–	1	–	1
	%			0,61						0,61
l_v^r/L^r		–	–	–	–	–	–	–	–	–
L_v^u/L^r		–	–	..	–	–	–	–	–	
L^u/L^u		2	–	2	–	–	–	2	–	2
	%			1,22						1,22
L_v^u/L^u		1	2	3	–	–		1	2	3
	%			1,83						1,83
L^u/T^r		–	–	–	–	–	–	–	–	–
L^u/L^c		–	–	–	–	–	–	–	–	–
W/l^r		– .	–	–	–	–	–	–	–	–
l^r/W		–	–	–	–	–	–	–	–	–
L^r/T^r		1	–	1	–	–	–	1	–	1
	%			0,61						0,61
$L^u/T^u/T^r$		–	–	–	–	–	–	–	–	–
L^r/L^u		1	1	2	–	–	–	1	1	2
	%			1,22						1,22
L^r/L^c		–	–	–	–	–	–	–	–	.
$L_v^u/L^u/L^u$		–	–	–	–	–	–	–	–	–
L_v^u/W		1	–	1	–	–	–	1	–	1
	%			0,61						0,61

	Muster			Spuren			Gesamt		
	r	l	r+l	r	l	r+l	r	l	r+l
	82	82	164	82	82	164	82	82	164
W_v/L_v^u	–	–	–	–	–	–	–	–	–
A^r/S	1	–	1	–	–	–	1	–	1
%			0,61						0,61
L^c/A^r	1	–	1	–	–	–	1	–	1
%			0,61						0,61
$L^u/l^u/L^u/L^u$	–	1	1	–	–	–	–	1	1
%			0,61						0,61
11 zusammenges. Muster %			10,37						10,37
18	44	46	90	16	11	27	60	57	117
%	53,66	56,10	54,89	19,51	13,41	16,47	73,17	69,51	71,36

Patienten (207 ♂♂ + 82 ♀♀)

Hypothenar ♂♂ + ♀♀

	Muster			Spuren			Gesamt		
	r 289	l 289	r+l 578	r 289	l 289	r+l 578	r 289	l 289	r+l 578
V	–	–	–	6	7	13	6	7	13
%						2,25			2,25
A^r	9	2	11	–	–	–	9	2	11
%			1,90						1,90
T^r	4	5	9	–	–	–	4	5	9
%			1,56						1,56
L^r	63	93	156	10	13	23	73	106	179
%			26,99			3,98			30,97
L^u	15	17	32	31	28	59	46	45	91
%			5,54			10,21			15,75
L^c	8	3	11	2	–	2	10	3	13
%			1,90			0,34			2,24
W	13	11	24	–	–	–	13	11	24
%			4,15						4,15
S	3	2	5	–	–	–	3	2	5
%			0,86						0,86
8 einfache Muster %			42,90			16,78			59,68
A^r/L^r, L^r/A^r	10	3	13	–	–	–	10	3	13
%			2,25						2,25
L^r/L^r	7	2	9	–	–	–	7	2	9
%			1,56						1,56
—	–	–	–	–	–	–	–	–	–
L^u_v/L^r, L^r/L^u	3	5	8	1	1	2	4	6	10
%			1,38			0,34			1,73
L^u/L^u, L^u_v/L^u	9	6	15	1	–	1	10	6	16
%			2,59			0,17			2,77
—				–	–	–	–	–	–
L^u/V^r	1	–	1	–	–	–	1	–	1
%			0,17						0,17
L^u/L^c	1	–	1	–	–	–	1	–	1
%			0,17						0,17
W/l^r	1	–	1	–	–	–	1	–	1
%			0,17						0,17
l^r/W	1	–	1	–	–	–	1	–	1
%			0,17						0,17
L^r/T^r	1	1	2	–	–	–	1	1	2
%			0,34						0,34
$L^u/V^u/V^r$	–	1	1	–	–	–	–	1	1
%			0,17						0,17

	Muster			Spuren			Gesamt		
	r	l	r+l	r	l	r+l	r	l	r+l
	289	289	578	289	289	578	289	289	578
—	–			–	–	·	–	–	–
L^r/L^c	1	1	2	–	–	–	1	1	2
%			0,34						0,34
$L^u_v/L^u/L^r$	–	1	1	–	–	–	–	1	1
%			0,17						0,17
$\left.\begin{array}{l} L/W \\ W_v/L_v \end{array}\right\}$	1	1	2	–	1	1	1	2	3
%			0,34			0,17			0,51
—		–	–	–	–	–	–	–	–
A^r/S	1	–	1	–	–	–	1	–	1
%			0,17						0,17
L^c/A^r	1	–	1	–	–	–	1	–	1
%			0,17						0,17
$L^u/l^u/L^u/L^u$	–	1	1	–	–	–	–	1	1
%			0,17						0,17
$\left.\begin{array}{l} L^r/V \\ V/L^r \end{array}\right\}$	1	1	2	–	–	–	1	1	2
%			0,34						0,34
L^r/l^m	1	–	1	–	–	–	1	–	1
%			0,17						0,17
23 zusammenges. Muster %			10,84			0,68			11,52
31	155	156	311	51	50	101	206	206	412
%	53,63	53,98	53,81	17,65	17,30	19,20	71,28	71,28	71,28

Patienten (207 ♂♂ + 82 ♀♀)

Thenar + 1 ♂♂

	Muster			Spuren			Gesamt		
	r	l	r+l	r	l	r+l	r	l	r+l
	207	207	414	207	207	414	207	207	414
V	–	–	–	26	30	56	26	30	56
%						13,53			13,53
L^c	4	–	4	2	–	2	6	–	6
%			0,97			0,48			1,45
L^r	1	9	10	2	1	3	3	10	13
%			2,40			0,72			3,12
W	–	3	3	–	–	–	–	3	3
%			0,72						0,72
q	–	1	1	–	–	–	–	1	1
%			0,24						0,24
Dv	–	–	–	1	–	1	1	–	1
%						0,24			0,24

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		207	207	414	207	207	414	207	207	414
L^r/L^r		–	2	2	1	–	1	1	2	3
	%			0,48			0,24			0,72
L^c/L^r		2	7	9	1	1	2	3	8	11
	%			2,17			0,48			2,65
L^c/Q		1	–	1	–	–	–	1	–	1
	%			0,24						0,24
Q/l^r		–	1	1	–	–	–	–	1	1
	%			0,24						0,24
$L^c/Q/L^r$		4	11	15	–	–	–	4	11	15
	%			3,62						3,62
$W/Q/L^r$		–	5	5	–	–	–	–	5	5
	%			1,21						1,21
12		12	39	51	33	32	65	45	71	116
	%	5,80	18,84	12,32	15,94	15,46	15,70	21,74	34,30	28,02

Thenar + 1 ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		82	82	164	82	82	164	82	82	164
V		–	–	–	6	10	16	6	10	16
	%						9,75			9,75
L^c		1	1	2	–	–	–	1	1	2
	%			1,22						1,22
L^r		–	1	1	2	1	3	2	2	4
	%			0,61			1,83			2,44
Q		–	1	1	–	–	–	–	1	1
	%			0,61						0,61
L^c/L^r		2	4	6	–	–	–	2	4	6
	%			3,66						3.66
L^c/Q		–	1	1	–	–	–	–	1	1
	%			0,61						0,61
Q/L^r		1	2	3	–	–	–	1	2	3
	%			1,83						1,83
$L^c/Q/L^r$		7	8	15	–	–	–	7	8	15
	%			9,15						9,15
$W/Q/L^r$		–	1	1	–	–	–	–	1	1
	%			0,61						0,61
9		11	19	30	8	11	19	19	30	49
	%	13,41	23,17	18,30	9,76	13,41	11,58	23,17	36,58	29,88

Thenar + 1 ♂♂ + ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		289	289	578	289	289	578	289	289	578
V		–	–	–	32	40	72	32	40	72
	%						12,46			12,46
L^c		5	1	6	2	–	2	7	1	8
	%			1,04			0,35			1,39
L^r		1	10	11	4	2	6	5	12	17
	%			1,90			1,04			2,94
W		–	3	3	–	–	–	–	3	3
	%			0,51						0,51
Dv		–	–	–	1	–	1	1	–	1
	%						0,17			0,17
Q, q		–	2	2	–	–	–	–	2	2
	%			0,35						0,35
L^r/L^r		–	2	2	1	–	1	1	2	3
	%			0,35			0,17			0,52
L^c/L^r		4	11	15	1	1	2	5	12	17
	%			2,59			0,35			2,94
L^c/Q		1	1	2	–	–	–	1	1	2
	%			0,35						0,35
Q/L^r		1	3	4	–	–	–	1	3	4
	%			0,70						0,70
$L^c/Q/L^r$		11	19	30	–	–	–	11	19	30
	%			5,19						5,19
$W/Q/L^r$		–	6	6	–	–	–	–	6	6
	%			1,04						1,04
12		23	58	81	41	43	84	64	101	165
	%	7,96	20,07	14,02	14,19	14,88	14,54	22,14	34,95	28,56

Patienten (207 ♂♂ + 82 ♀♀)

JII ♂♂

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		207	207	414	207	207	414	207	207	414
d/dv		1	–	1	–	–	–	1	–	1
	%			0,24						0,24
d		1	–	1	11	2	13	12	2	14
	%			0,24			3,14			3,38
D		14	7	21	9	3	12	23	10	33
	%			5,07			2,90			7,97
3		16	7	23	20	5	25	36	12	48
	%	7,73	3,38	5,55	9,66	2,41	6,04	17,39	5,80	11,59

JII ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		82	82	164	82	82	164	82	82	164
d/dv		–	–	–	–	–	–	–	–	–
d		–	–	–	–	2	2	–	2	2
	%						1,22			1,22
D		4	1	5	4	1	5	8	2	10
	%			3,05			3,05			6,10
2		4	1	5	4	3	7	8	4	12
	%	4,88	1,22	3,05	4,88	3,66	4,27	9,76	4,88	7,32

JII ♂♂ + ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		289	289	578	289	289	578	289	289	578
d/dv		1	–	1	–	–	–	1	–	1
	%			0,17						0,17
d		1	–	1	11	4	15	12	4	16
	%			0,17			2,59			2,77
D		18	8	26	13	4	17	31	12	43
	%			4,50			2,94			7,44
3		20	8	28	24	8	32	44	16	60
	%	6,92	2,77	4,84	8,30	2,77	5,54	15,22	5,54	10,38

Patienten (207 ♂♂ + 82 ♀♀)

JIII ♂♂

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		207	207	414	207	207	414	207	207	414
L, l		110	52	162	8	15	23	118	67	185
	%	53,14	25,12	39,13	3,86	7,25	5,55	57,00	32,37	44,49

JIII ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		82	82	164	82	82	164	82	82	164
L, l		48	23	71	3	3	6	51	26	77
	%			43,29			3,66			46,95
d		–	–	–	1	–	1	1	–	1
	%						0,61			0,61
D		–	–	–	1	–	1	1	–	1
	%						0,61			0,61
3		48	23	71	5	3	8	53	26	79
	%	58,54	28,05	43,29	6,10	3,66	4,88	64,63	31,71	48,17

JIII ♂♂ + ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		289	289	578	289	289	578	289	289	578
L, l		158	75	233	11	18	29	169	93	262
	%			40,51			5,02			45,33
d		–	–	–	1	–	1	1	–	1
	%						0,17			0,17
D		–	–	–	1	–	1	1	–	1
	%						0,17			0,17
3		158	75	233	13	18	31	171	93	264
	%	54,67	25,95	40,51	4,50	6,23	5,36	59,17	32,18	45,67

Patienten (207 ♂♂ + 82 ♀♀)

JIV ♂♂

	Muster			Spuren			Gesamt		
	r	l	r+l	r	l	r+l	r	l	r+l
	207	207	414	207	207	414	207	207	414
V	–	–	–	–	3	3	–	3	3
%						0,72			0,72
L, l	53	75	128	7	8	15	60	83	143
%			30,92			3,62			34,54
D, d	19	18	37	24	22	46	43	40	83
%			8,94			11,11			20,05
W	1	–	1	–	–	–	1	–	1
%			0,24						0,24
D/L, L/D	5	22	27	1	1	2	6	23	29
%			6,52			0,48			7,00
L–L′	–	1	1	–	–	–	–	1	1
%			0,24						0,24
dv/Dv	–	–	–	1	–	1	1	–	1
%						0,24			0,24
L/V	–	1	1	–	–	–	–	1	1
%			0,24						0,24
	78	117	195	33	34	67	111	151	262
%	37,68	56,52	47,10	15,94	16,42	16,17	59,62	72,95	63,27

JIV ♀♀

	Muster			Spuren			Gesamt		
	r	l	r+l	r	l	r+l	r	l	r+l
	82	82	164	82	82	164	82	82	164
V	–	–	–	–	–	–	–	–	–
L, l	19	31	50	3	3	6	22	34	56
%			30,49			3,66			34,15
D	3	3	6						
d	3	3	6	9	6	15	15	12	27
%			7,32			9,15			16.47
L/D	–	3	3	1	1	2	1	4	5
%			1,83			1,22			3,05
	25	40	65	13	10	23	38	50	88
%	30,49	48,78	39,64	15,85	12,19	14,03	46,34	60,98	53,67

JIV ♂♂ + ♀♀

		Muster			Spuren			Gesamt	
	r	l	r+l	r	l	r+l	r	l	r+l
	289	289	578	289	289	578	289	289	578
V	–	–	–	–	3	3	–	3	3
%						0,51			0,51
L, l	72	106	178	10	11	21	82	117	199
%			30,80			3,63			34,43
D, d	25	24	49	33	28	61	58	52	110
%			8,48			10,55			19,03
W	1	–	1	–	–	–	1	–	1
%			0,17						0,17
L/D, D/L	5	25	30	2	2	4	7	27	34
%			5,19			0,69			5,88
L–L′	–	1	1	–	–	–	–	1	1
%			0,17						0,17
dv/Dv	–	–	–	1	–	1	1	–	1
%						0,17			0,17
L/V	–	1	1	–	–	–	–	1	1
%			0,17						0,17
	103	157	260	46	44	90	149	201	350
%	35,64	54,32	44,98	15,92	15,22	15,55	51,56	69,55	60,63

Zwillinge (Normalbevölkerung) 83 ♂♂ + 104 ♀♀
Hypothenar ♂♂

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		83	83	166	83	83	166	83	83	166
A^r		2	–	2	–	–	–	2	–	2
	%			1,20						1,20
T^u		1	–	1	–	–	–	1	–	1
	%			0,60						0,60
T^r		1	–	1	–	–	–	1	–	1
	%			0,60						0,60
L^r / l^r		16	19	35	2	3	5	18	22	40
	%			21,08			3,01			24,10
L^u		3	4	7	6	5	11	9	9	18
	%			4,22			6,63			10,84
L^c		–	1	1	–	–	–	–	1	1
	%			0,60						0,60
W		4	1	5	–	–	–	4	1	5
	%			3,01						3,01
V		–	–	–	–	1	1	–	1	1
	%						0,60			0,60
9 einfache Muster	%			31,31			10,24			41.55
A^r/L^r / L^r/A^r		5	–	5	–	–	–	5	–	5
	%			3,01						3,01
A^r/L^c		1	–	1	–	–	–	1	–	1
	%			0,60						0,60
L^r/L^u / L^u/L^r		1	1	2	–	–	–	1	1	2
	%			1,20						1,20
L^r_v/L^c		–	1	1	–	–	–	–	1	1
	%			0,60						0,60
L^u_v/L^c		1	–	1	–	–	–	1	–	1
	%			0,60						0,60
W/L^u		1	–	1	–	–	–	1	–	1
	%			0,60						0,60
$L^r/L^r/L^u$		–	1	1	–	–	–	–	1	1
	%			0,60						0,60
9 zusammenges. Muster	%			7,21						7,21
18		36	28	64	8	9	17	44	37	81
	%	43,37	33,37	38,52	9,64	10,84	10,24	53,01	44,58	48,76

Zwillinge (Normalbevölkerung) 83 ♂♂ + 104 ♀♀
Hypothenar ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		104	104	208	104	104	208	104	104	208
A^r		3	–	3	–	–	–	3	–	3
	%			1,44						1,44
T^r		1	1	2	–	–	–	1	1	2
	%			0,96						0,96
T^u		1	1	2	–	–	–	1	1	2
	%			0,96						0,96
l^r } L^r		27	27	54	2	5	7	29	32	61
	%			25,96			3,36			29,32
L^u		5	7	12	5	4	9	10	11	21
	%			5,77			4,33			10,10
L^c		4	2	6	–	–	–	4	2	6
	%			2,88						2,88
W		5	6	11	–	–	–	5	6	11
	%			5,29						5,29
V		–	–	–	1	2	3	1	2	3
	%						1,44			1,44
9 einfache Muster	%			43,26			9,13			52,39
L^r/A^r } $A^r\ L^r$		2	1	3	–	–	–	2	1	3
	%			1,44						1,44
L^r/L^u		1	1	2	–	–	–	1	1	2
	%			0,96						0,96
L^u_v/L^u		1	1	2	–	–	–	1	1	2
	%			0,96						0,96
L^u/L^c		1	–	1	–	–	–	1	–	1
	%			0,48						0,48
L^r/L^r		1	–	1	–	–	–	1	–	1
	%			0,48						0,48
L^r/W		–	1	1	–	–	–	–	1	1
	%			0,48						0,48
W/A^r		1	–	1	–	–	–	1	–	1
	%			0,48						0,48
W/T^u		2	–	2	–	–	–	2	–	2
	%			0,96						0,96
$L^u/L^r/L^u$		–	1	1	–	–	–	–	1	1
	%			0,48						0,48
10 zusammenges. Muster	%			6,72						6,72
19		55	49	104	8	11	19	63	60	123
	%	52,88	47,11	50,00	7,69	10,58	9,13	60,58	57,69	59,13

Zwillinge (Normalbevölkerung) 83 ♂♂ + 104 ♀♀

Hypothenar ♂♂ + ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		187	187	374	187	187	374	187	187	374
A^r		5	–	5	–	–	–	5	–	5
	%			1,34						1,34
T^u		2	1	3	–	–	–	2	1	3
	%			0,80						0,80
T^r		2	1	3	–	–	–	2	1	3
	%			0,80						0,80
l^r, L^r		43	46	89	4	8	12	47	54	101
	%			23,80			3,21			27,01
L^u		8	11	19	11	9	20	19	20	39
	%			5,08			5,35			10,43
L^c		4	3	7	–	–	–	4	3	7
	%			1,87						1,87
W		9	7	16	–	–	–	9	7	16
	%			4,28						4,28
V		–	–	–	1	3	4	1	3	4
	%						1,07			1,07
9 einfache Muster	%			37,97			9,63			47,60
L^r/A^r, A^r/L^r		7	1	8	–	–	–	7	1	8
	%			2,14						2,14
L^r/L^r		1	–	1	–	–	–	1	–	1
	%			0,27						0,27
L^r/L^u, L^u/L^r		2	2	4	–	–	–	2	2	4
	%			1,07						1,07
L^u_v/L^u		2	–	2	–	–	–	2	–	2
	%			0,54						0,54
A^r/L^c		1	–	1	–	–	–	1	–	1
	%			0,27						0,27
L^r_v/L^c		–	1	1	–	–	–	–	1	1
	%			0,27						0,27
L^u/L^c, L^c/L^u		1	1	2	–	–	–	1	1	2
	%			0,54						0,54
W/L^u		1	–	1	–	–	–	1	–	1
	%			0,27						0,27
L^r/W		–	1	1	–	–	–	–	1	1
	%			0,27						0,27
W/A^r, W/T^u		3	–	3	–	–	–	3	–	3
	%			0,80						0,80
$L^r/L^r/L^u$, $L^u/L^r/L^u$		–	2	2	–	–	–	–	2	2
	%			0,54						0,54
16 zusammenges. Muster	%			6,98						6,98
25		91	77	168	16	20	36	107	97	204
	%	48,60	41,18	44,95	8,56	10,69	9,63	57,22	51,87	54,58

Zwillinge (Normalbevölkerung) 83 ♂♂ + 104 ♀♀

Thenar + 1 ♂♂

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		83	83	166	83	83	166	83	83	166
L^r		1	2	3	–	–	–	1	2	3
	%			1,81						1,81
L^c		–	–	–	–	1	1	–	1	1
	%						0,60			0,60
V		–	–	–	3	8	11	3	8	11
	%						6,63			6,63
Q		2	–	2	–	–	–	2	–	2
	%			1,20						1,20
L^c/L^r		1	1	2	–	–	–	1	1	2
	%			1,20						1,20
$L^c/Q/L^r$		2	8	10	–	–	–	2	8	10
	%			6,02						6,02
$W/Q/L^r$		–	2	2	–	–	–	–	2	2
	%			1,20						1,20
7		6	13	19	3	9	12	9	22	31
	%	7,23	15,66	11,45	3,61	10,84	7,22	10,84	26,51	18,67

Thenar + 1 ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		104	104	208	104	104	208	104	104	208
L^c		1	–	1	1	–	1	2	–	2
	%			0,48			0,48			0,96
V		–	–	–	4	2	6	4	2	6
	%						2,88			2,88
Q/l^r		–	1	1	–	–	–	–	1	1
	%			0,48						0,48
L^c/L^r		3	2	5	–	–	–	3	2	5
	%			2,40						2,40
$L^c/Q/L^r$		5	8	13	–	–	–	5	8	13
	%			6,25						6,25
$W/Q/L^r$		1	2	3	–	–	–	1	2	3
	%			1,44						1,44
6		10	13	23	5	2	7	15	15	30
	%	9,61	12,50	11,06	4,81	1,92	3,36	14,42	14,42	14,42

Thenar + 1 ♂♂ + ♀♀

		Muster			Spuren			Gesamt		
		r 187	l 187	r+l 374	r 187	l 187	r+l 374	r 187	l 187	r+l 374
V		–	–	–	7	10	17	7	10	17
	%						4,54			4,54
L^r		1	2	3	–	–	–	1	2	3
	%			0,80						0,80
L^c		1	–	1	1	1	2	2	1	3
	%			0,27			0,53			0,80
Q		2	–	2	–	–	–	2	–	2
	%			0,53						0,53
Q/L		–	1	1	–	–	–	–	1	1
	%			0,27						0,27
L^c/L^r		4	3	7	–	–	–	4	3	7
	%			1,87						1,87
$L^c/Q/L^r$		7	16	23	–	–	–	7	16	23
	%			6,15						6,15
$W/Q/L^r$		1	4	5	–	–	–	1	4	5
	%			1,34						1,34
8		16	26	42	8	11	19	24	37	61
	%	8,56	13,90	11,23	4,28	5,88	5,08	13,04	20,11	16,31

Zwillinge (Normalbevölkerung) 83 ♂♂ + 104 ♀♀

JII ♂♂

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		83	83	166	83	83	166	83	83	166
V		–	–	–	1	–	1	1	–	1
	%						0,60			0,60
d		2	2	4	1	–	1	3	2	5
	%			2,41			0,60			3,01
D		6	4	10	1	–	1	7	4	11
	%			6,02			0,60			6,63
		8	6	14	3	–	3	11	6	17
	%	9,64	7,23	8,43	3,61	–	1,81	13,25	7,23	10,24

JII ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		104	104	208	104	104	208	104	104	208
V		–	–	–	–	–	–	–	–	–
	%									
d		1	1	2	2	1	3	3	2	5
	%			0,96			1,44			2,40
D		2	–	2	–	1	1	2	1	3
	%			0,96			0,48			1,44
		3	1	4	2	2	4	5	3	8
	%	2,88	0,96	1,92	1,92	1,92	1,92	4,81	2,88	3,85

JII ♂♂ + ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		187	187	374	187	187	374	187	187	374
V		–	–	–	1	–	1	1	–	1
	%						0,27			0,27
d		3	3	6	3	1	4	6	4	10
	%			1,60			1,07			2,67
D		8	4	12	1	1	2	9	5	14
	%			3,20			0,54			3,74
		11	7	18	5	2	7	16	9	25
	%	5,88	3,74	4,81	2,67	1,07	1,87	8,56	4,81	6,68

Zwillinge (Normalbevölkerung) 83 ♂♂ + 104 ♀♀

JIII ♂♂

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		83	83	166	83	83	166	83	83	166
L l		36	13	49	2	7	9	38	20	58
	%			29,52			5,42			34,94
V		–	–	–	–	1	1	–	1	1
	%						0,60			0,60
		36	13	49	2	8	10	38	21	59
	%	43,37	15,66	29,52	1,20	9,64	6,02	45,78	25,30	35,54

JIII ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		104	104	208	104	104	208	104	104	208
L l		42	35	77	2	4	6	44	39	83
	%			37,02			2,88			39,90
d		–	–	–	1	–	1	1	–	1
	%						0,48			0,48
D		1	–	1	–	–	–	1	–	1
	%			0,48						0,48
W		1	1	2	–	–	–	1	1	2
	%			0,96						0,96
		44	36	80	3	4	7	47	40	87
	%	42,31	34,61	38,46	2,88	3,85	3,36	45,19	38,46	41,83

JIII ♂♂ + ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		187	187	374	187	187	374	187	187	374
V		–	–	–	–	1	1	–	1	1
	%						0,27			0,27
L l		78	48	126	4	11	15	82	59	141
	%			33,69			4,01			37,70
d D		1	–	1	1	–	1	2	–	2
	%			0,27			0,27			0,54
W		1	1	2	–	–	–	1	1	2
	%			0,54						0,54
		80	49	129	5	12	17	85	61	146
	%	42,78	26,20	34,50	2,67	6,42	4,54	45,45	32,62	39,04

Zwillinge (Normalbevölkerung) 83 ♂♂ + 104 ♀♀

JIV ♂♂

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		83	83	166	83	83	166	83	83	166
V		–	–	–	–	1	1	–	1	1
	%						0,60			0,60
L l		29	31	60	1	3	4	30	34	64
	%			36,14			2,41			38,55
d D		9	12	21	6	9	15	15	21	36
	%			12,65			9,04			21,69
L/D		–	5	5	–	–	–	–	5	5
	%			6,02						6,02
W		–	2	2	–	–	–	–	2	2
	%			1,20						1,20
		38	50	88	7	13	20	45	63	108
	%	45,78	60,24	53,01	8,43	15,66	12,05	54,22	75,90	65,06

JIV ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		104	104	208	104	104	208	104	104	208
V		–	–	–	3	2	5	3	2	5
	%						2,40			2,40
L l		43	34	77	2	3	5	45	37	82
	%			37,02			2,40			39,42
d D		8	16	24	9	4	13	17	20	37
	%			11,54			6,25			17,79
L/D D/L		–	5	5	–	–	–	–	5	5
	%			2,40						2,40
W		1	2	3	–	–	–	1	2	3
	%			1,44						1,44
		52	57	109	14	9	23	66	66	132
	%	50,00	54,81	52,40	13,46	8,65	11,06	63,46	63,46	63,46

JIV-♂♂ + ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		187	187	374	187	187	374	187	187	374
V		–	–	–	3	3	6	3	3	6
	%						1,60			1,60
L, l		72	65	137	3	6	9	75	71	146
	%			36,63			2,41			39,04
d, D		17	28	45	15	13	28	32	41	73
	%			12,03			7,49			19,52
L/D, D/L		–	10	10	–	–	–	–	10	10
	%			2,67						2,67
W		1	4	5	–	–	–	1	4	5
	%			1,34						1,34
		90	107	197	21	22	43	111	129	240
	%	48,13	57,22	52,67	11,23	11,76	11,50	59,36	68,98	64,17

Marburger Normalbevölkerung (300 ♂♂ + 300 ♀♀)
Hypothenar ♂♂

	Muster			Spuren			Gesamt		
	r 300	l 300	r+l 600	r 300	l 300	r+l 600	r 300	l 300	r+l 600
L^d	–	2	2	–	–	–	–	2	2
%			0,34						0,34
V	–	–	–	2	4	6	2	4	6
%						1,00			1,00
A^r	5	3	8	–	–	–	5	3	8
%			1,33						1,33
T^r	1	1	2	–	–	–	1	1	2
%			0,34						0,34
L^r	52	60	112	3	4	7	55	64	119
%			18,67			1,17			19,84
L^u	23	23	46	21	16	37	44	39	83
%			7,67			6,17			13,84
L^c	3	2	5	–	–	–	3	2	5
%			0,83						0,83
W	9	5	14	–	–	–	9	5	14
%			2,33						2,33
S	2	6	8	–	–	–	2	6	8
%			1,33						1,33
9 einfache Muster %			32,84			8,34			41,18
V/L^d	1	–	1	–	–	–	1	–	1
%			0,17						0,17
A^r/L^u	1	1	2	–	–	–	1	1	2
%			0,34						0,34
A^r/L^c	1	–	1	–	–	–	1	–	1
%			0,17						0,17
l^r/A^r	2	2	4	–	–	–	2	2	4
%			0,66						0,66
L^r/L^r	4	–	4	–	–	–	4	–	4
%			0,66						0,66
L^r/L^u	4	4	8	–	–	–	4	4	8
%			1,33						1,33
L^r/W^r	1	–	1	–	–	–	1	–	1
%			0,17						0,17
L^u/L^u	1	2	3	–	–	–	1	2	3
%			0,50						0,50
L^c/L^u	–	1	1	–	–	–	–	1	1
%			0,17						0,17
T^r/L^r	1	–	1	–	–	–	1	–	1
%			0,17						0,17
T^r/L^d	1	–	1	–	–	–	1	–	1
%			0,17						0,17
$L^r/A^r/T^d$	–	1	1	–	–	–	–	1	1
%			0,17						0,17
12 zusammenges. Muster %			4,68						4,68
21	112	113	225	26	24	50	132	137	275
%	37,33	37,67	37,52	8,67	8,00	8,34	46,00	45,67	45,86

Marburger Normalbevölkerung (300 ♂♂ + 300 ♀♀)

Hypothenar ♀♀

		Muster			Spuren			Gesamt		
		r 300	l 300	r+l 600	r 300	l 300	r+l 600	r 300	l 300	r+l 600
L^d		5	–	5	–	–	–	5	–	5
	%			0,83						0,83
V		–	–	–	3	1	4	3	1	4
	%						0,66			0,66
A^r		10	3	13	–	–	–	10	3	13
	%			2,17						2,17
T^r		2	1	3	–	–	–	2	1	3
	%			0,50						0,50
L^r		57	76	133	2	4	6	59	80	139
	%			22,17			1,00			23,17
L^u		30	21	51	12	16	28	42	37	79
	%			8,50			4,76			13,26
L^c		7	4	11	–	1	1	7	5	12
	%			1,83			0,17			2,00
W		14	4	18	–	1	1	14	5	19
	%			3,00			0,17			3,17
S		1	6	7	–	–	–	1	6	7
	%			1,17						1,17
9 einfache Muster	%			40,17			6,76			46,93
A^r/L^u		1	–	1	–	–	–	1	–	1
	%			0,17						0,17
A^r/L^c		2	–	2	–	–	–	2	–	2
	%			0,34						0,34
L^r/A^r		4	2	6	–	–	–	4	2	6
	%			1,00						1,00
L^r/L^r		–	1	1	–	–	–	–	1	1
	%			0,17						0,17
L^r/L^u		3	2	5	–	–	–	3	2	5
	%			0,83						0,83
L^r/W_v		–	–	–	–	–	–	–	–	–
L^u/L^u		3	4	7	–	–	–	3	4	7
	%			1,17						1,17
L^u/L^c		–	1	1	–	–	–	–	1	1
	%			0,17						0,17
T^r/L^r		–	–	–	–	–	–	–	–	–
T^r/L^d		–	–	–	–	–	–	–	–	–
$L^r/A^r/T^d$		–	–	–	–	–	–	–	–	–
L^r/L^d		1		1				1		1
	%			0,17						0,17
W/L^u		–	1	1	–	–	–	–	1	1
	%			0,17						0,17
9 zusammenges. Muster	%			4,19						4,19
18		140	126	266	17	23	40	157	149	306
	%	46,67	42,00	44,36	5,67	7,67	6,76	52,33	49,67	51,12

Marburger Normalbevölkerung (300 ♂♂ + 300 ♀♀)
Hypothenar ♂♂ + ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		600	600	1200	600	600	1200	600	600	1200
L^d		5	2	7	–	–	–	5	2	7
	%			0,58						0,58
V		–	–	–	5	5	10	5	5	10
	%						0,83			0,83
A^r		15	6	21	–	–	–	15	6	21
	%			1,75						1,75
T^r		3	2	5	–	–	–	3	2	5
	%			0,42						0,42
L^r		109	136	245	5	8	13	114	144	258
	%			20,42			1,08			21,50
L^u		53	44	97	33	32	65	84	75	159
	%			8,08			5,42			13,50
L^c		10	6	16	–	1	1	10	7	17
	%			1,33			0,08			1,42
W		23	9	32	–	1	1	23	10	33
	%			2,67			0,08			2,75
S		3	12	15	–	–	–	3	12	15
	%			1,25						1,25
9 einfache Muster	%			36,50			7,49			43,99
V/L^d		1	–	1	–	–	–	1	–	1
	%			0,08						0,08
A^r/L^u		1	1	3	–	–	–	2	1	3
	%			0,25						0,25
A^r/L^c		3	–	3	–	–	–	3	–	3
	%			0,25						0,25
L^r/A^r		6	4	10	–	–	–	6	4	10
	%			0,83						0,83
L^r/L^r		4	1	5	–	–	–	4	1	5
	%			0,42						0,42
L^r/L^u		7	6	13	–	–	–	7	6	13
	%			1,08						1,08
L^r/W_v		1	–	1	–	–	–	1	–	1
	%			0,08						0,08
L^u/L^u		4	6	10	–	–	–	4	6	10
	%			0,83						0,83
L^u/L^c		–	1	1	–	–	–	–	1	1
	%			0,08						0,08
L^c/L^u		–	1	1	–	–	–	–	1	1
	%			0,08						0,08
T^r/L^r		1	–	1	–	–	–	1	–	1
	%			0,08						0,08
T^r/L^d		1	–	1	–	–	–	1	–	1
	%			0,08						0,08

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		600	600	1200	600	600	1200	600	600	1200
$L^r/A^r/T^d$		–	1	1	–	–	–	–	1	1
	%			0,08						0,08
W/L^u		–	1	1	–	–	–	–	1	1
	%			0,08						0,08
L^r/L^d		1	–	1	–	–	–	1	–	1
	%			0,08						0,08
15 zusammenges. Muster	%			4,38						4,38
24		252	239	491	43	47	90	292	286	578
	%	42,00	39,83	40,88	7,17	7,86	7,49	48,67	47,67	48,37

Marburger Normalbevölkerung (300 ♂♂ + 300 ♀♀)

Thenar + 1 ♂♂

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		300	300	600	300	300	600	300	300	600
V		–	–	–	9	12	21	9	12	21
	%						3,50			3,50
L^r		–	2	2	1	7	8	1	9	10
	%			0,34			1,33			1,67
L^c		1	1	2	–	–	–	1	1	2
	%			0,34						0,34
W } Q }		–	–	–	–	–	–	–	–	–
L^r/Q } Q/L^r }		3	8	11	–	–	–	3	8	11
	%			1,83						1,83
L^c/Q		2	–	2	–	–	–	2	–	2
	%			0,34						0,34
L^c/L^r		1	3	4	–	–	–	1	3	4
	%			0,66						0,66
$L^c/Q/L^r$		8	23	31	–	–	–	8	23	31
	%			5,17						5,17
L^cQ/V		2	2	4	–	–	–	2	2	4
	%			0,66						0,66
$W/Q/L^r$		1	1	2	–	–	–	1	1	1
	%			0,34						0,34
		18	40	58	10	19	29	28	59	87
	%	6,00	13,33	9,67	3,33	6,33	4,83	9,33	19,67	14,50

Thenar + 1 ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		300	300	600	300	300	600	300	300	600
V		–	–	–	6	7	13	6	7	13
	%						2,17			2,17
L^r		–	–	–	–	3	3	–	3	3
	%						0,50			0,50
L^c		–	1	1	–	–	–	–	1	1
	%			0,17						0,17
W		–	1	1	–	–	–	–	1	1
	%			0,17						0,17
Q		1	–	1	–	–	–	1	–	1
	%			0,17						0,17
Q/L^r		1	5	6	–	–	–	1	5	6
	%			1,00						1,00
L^c/Q		1	1	2	–	–	–	1	1	2
	%			0,34						0,34
L^c/L^r		1	1	2	–	–	–	1	1	2
	%			0,34						0,34
$L^c/Q/L^r$		14	23	37	–	–	–	14	23	37
	%			6,17						6,17
$L^c/Q/V$		1	–	1	–	–	–	1	–	1
	%			0,17						0,17
$W/Q/L^r$		1	–	1	–	–	–	1	–	1
	%			0,17						0,17
$L^c/Q/L^r/l^c$		1	1	2	–	–	–	1	1	2
	%			0,34						0,34
		21	33	54	6	10	16	27	43	70
	%	7,00	11,00	9,00	2,00	3,33	2,67	9,00	14,33	11,67

Marburger Normalbevölkerung (300 ♂♂ 300 ♀♀)
Thenar + 1 ♂♂ + ♀♀

	Muster			Spuren			Gesamt		
	r 600	l 600	r+l 1200	r 600	l 600	r+l 1200	r 600	l 600	r+l 1200
V	–	–	–	15	19	34	15	19	34
%						2,83			2,83
L^r	–	2	2	1	10	11	1	12	13
%			0,17			0,92			1,08
L^c	1	2	3	–	–	–	1	2	3
%			0,25						0,25
W	–	1	1	–	–	–	–	1	1
%			0,08						0,08
Q	1	–	1	–	–	–	1	–	1
%			0,08						0,08
L^r/Q } Q/L^r }	4	13	17	–	–	–	4	13	17
%			1,42						1,42
L^c/Q	3	1	4	–	–	–	3	1	4
%			0,33						0,33
L^c/L^r	2	4	6	–	–	–	2	4	6
%			0,50						0,50
$L^c/Q/L^r$	22	46	68	–	–	–	22	46	68
%			5,67						5,67
$L^c/Q/V$	3	2	5	–	–	–	3	2	5
%			0,42						0,42
$W/Q/L^r$	2	1	3	–	–	–	2	1	3
%			0,25						0,25
$L^c/Q/L^r/l^r$	1	1	2	–	–	–	1	1	2
%			0,17						0,17
	39	73	112	16	29	45	55	102	157
%	6,50	12,17	9,33	2,67	4,83	3,75	9,17	17,00	13,08

Marburger Normalbevölkerung (300 ♂♂ + 300 ♀♀)

JII ♂♂

	Muster			Spuren			Gesamt		
	r	l	r+l	r	l	r+l	r	l	r+l
	300	300	600	300	300	600	300	300	600
d	1	–	1	3	1	4	4	1	5
%			0,17			0,67			0,83
D	21	6	27	4	4	8	25	10	35
%			4,50			1,34			5,83
V	–	–	–	2	2	4	2	2	4
%						0,67			0,67
	22	6	28	9	7	16	31	13	44
%	7,33	2,00	4,67	3,00	2,33	2,67	10,33	4,33	7,33

JII ♀♀

	Muster			Spuren			Gesamt		
	r	l	r+l	r	l	r+l	r	l	r+l
	300	300	600	300	300	600	300	300	600
d	–	–	–	2	–	2	2	–	2
%						0,34			0,34
D	6	5	11	6	–	6	12	5	17
%			1,83			1,00			2,83
V	–	–	–	1	2	3	1	2	3
%						0,50			0,50
	6	5	11	9	2	11	15	7	22
%	2,00	1,67	1,83	3,00	0,67	1,83	5,00	2,33	3,67

JII ♂♂ + ♀♀

	Muster			Spuren			Gesamt		
	r	l	r+l	r	l	r+l	r	l	r+l
	600	600	1200	600	600	1200	600	600	1200
d	1	–	1	5	1	6	6	1	7
%			0,08			0,50			0,58
D	27	11	38	10	4	14	37	15	52
%			3,17			1,17			4,33
V	–	–	–	3	4	7	3	4	7
%						0,58			0,58
	28	11	39	18	9	27	46	20	66
%	4,67	1,83	3,25	3,00	1,50	2,25	7,67	0,33	5,50

Marburger Normalbevölkerung (300 ♂♂ + 300 ♀)

JIII ♂♂

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		300	300	600	300	300	600	300	300	600
L/l		166	98	264	2	2	4	168	100	268
	%			44,00			0,67			44,67
D		4	1	5	1	–	1	5	1	6
	%			0,83			0,17			1,00
V		–	–	–	2	1	3	2	1	3
	%						0,50			0,50
		170	99	269	5	3	8	175	102	277
	%	56,67	33,00	44,83	1,67	1,00	1,33	58,33	34,00	46,17

JIII ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		300	300	600	300	300	600	300	300	600
L/l		143	72	215	1	2	3	144	74	218
	%			35,83			0,50			36,33
D		5	2	7	–	–	–	5	2	7
	%			1,17						1.17
V		–	–	–	1	–	1	1	–	1
	%						0,17			0,17
W		1	–	1	–	–	–	1	–	1
	%			0,17						0.17
		149	74	223	2	2	4	151	76	227
	%	49,67	24,67	37,17	0,67	0,67	0,67	50,33	25,33	37,83

JIII ♂♂ + ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		600	600	1200	600	600	1200	600	600	1200
L } l		309	170	479	3	4	7	312	174	486
	%			39,92			0,58			40,50
D		9	3	12	1	–	1	10	3	13
	%			1,00			0,08			1,08
V		–	–	–	3	1	4	3	1	4
	%						0,33			0,33
W		1	–	1	–	–	–	1	–	1
	%			0,08						0,08
		319	173	492	7	5	12	326	178	504
	%	53,17	28,83	41,00	1,17	0,83	1,00	54,33	89,67	42,00

Marburger Normalbevölkerung (300 ♂♂ + 300 ♀♀)
JIV ♂♂

	Muster			Spuren			Gesamt		
	r 300	l 300	r+l 600	r 300	l 300	r+l 600	r 300	l 300	r+l 600
l, L	93	114	207	–	1	1	93	115	208
%			34,50			0,17			34,67
d, D	26	36	62	10	18	28	36	54	90
%			10,33			4,67			15,00
W	2	3	5	–	1	1	2	4	6
%			0,83			0,17			1,00
V	–	–	–	5	3	8	5	3	8
%						1,33			1,33
L/D, D/L	1	13	14	–	1	1	1	14	15
%			2,33			0,17			2,50
L/Dv	–	13	13	–	–	–	–	13	13
%			2,17						2,17
L/W	1	–	1	–	–	–	1	–	1
%			0,17						0,17
L/V, V/L	–	3	3	–	–	–	–	3	3
%			0,50						0,50
l/l	–	1	1	–	–	–	–	1	1
%			0,17						0,17
D/W	–	2	2	–	–	–	–	2	2
%			0,34						0,34
D/D	–	1	1	–	–	–	–	1	1
			0,17						0,17
L_v/L_v^u	–	–	–	–	–	–	–	–	–
	123	186	309	15	24	39	138	210	348
%	41,00	62,00	51,50	5,00	8,00	6,50	46,00	70,00	58,00

JIV ♀♀

		Muster			Spuren			Gesamt		
		r	l	r+l	r	l	r+l	r	l	r+l
		300	300	600	300	300	600	300	300	600
l, L		120	141	261	–	1	1	120	141	261
	%			43,50			0,17			43,67
d, D		29	33	62	12	18	30	41	51	92
	%			10,33			5,10			15,33
W		–	1	1	–	–	–	–	1	1
	%			0,17						0,17
V		–	–	–	3	4	7	3	4	7
	%						1,17			1,17
L/D		4	9	13	–	–	–	4	9	13
	%			2,17						2,17
L/Dv		1	8	9	–	–	–	1	8	9
	%			1,50						1,50
L/W		–	1	1	–	–	–	–	1	1
	%			0,17						0,17
L/V		1	1	2	–	–	–	1	1	2
	%			0,34						0,34
l/L		–	1	1	–	–	–	–	1	1
	%			0,17						0,17
l/l		–	–	–	–	–	–	–	–	–
D/W		–	–	–	–	–	–	–	–	–
D/D		–	–	–	–	–	–	–	–	–
L_v/L_v^n		–	–	–	–	1	1	–	1	1
	%						0,17			0,17
		155	195	350	15	24	39	170	219	389
	%	51,67	65,00	58,33	5,00	8,00	6,50	56,67	73,00	64,83

JIV ♂♂ + ♀♀

	Muster			Spuren			Gesamt		
	r 600	l 600	r+l 1200	r 600	l 600	r+l 1200	r 600	l 600	r+l 1200
l L	213	255	468	–	2	2	213	257	470
%			39,00			0,17			39,17
d D	55	69	124	22	36	58	77	105	182
%			10,33			4,83			15,17
W	2	4	6	–	1	1	2	5	7
%			0,50			0,08			0,58
V	–	–	–	8	7	15	8	7	15
%						1,25			1,25
L/D D/L	5	22	27	–	1	1	5	23	28
%			2,25			0,08			2,33
L/Dv	1	21	22	–	–	–	1	21	22
%			1,83						1,83
L/W	1	1	2	–	–	–	1	1	2
%			0,17						0,17
L/V V/L	1	4	5	–	–	–	1	4	5
%			0,42						0,42
l/l l/l	–	2	2	–	–	–	–	2	2
%			0,17						0,17
D/W	–	2	2	–	–	–	–	2	2
%			0,17						0,17
D/D	–	1	1	–	–	–	–	1	1
%			0,08						0,08
Lv/Lv	–	–	–	–	1	1	–	1	1
%						0,08			0,08
	278	381	659	30	48	78	308	429	737
%	46,33	63,50	54,92	5,00	8,00	6,50	51,33	71,50	61,42

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DIE FINGERLEISTENMUSTER IN IHRER BEZIEHUNG ZU CEREBRALEN STÖRUNGEN[1]

VON WALTER HIRSCH

Die meisten Untersuchungen, die nach Beziehungen zwischen dem Tastleistensystem der Haut und cerebralen Störungen gesucht haben, beziehen sich auf die Papillarmuster auf den *Fingerbeeren*. Viele der veröffentlichten Ergebnisse haben aber einer kritischen Nachprüfung nicht standgehalten. *G. G. Wendt* hat jedenfalls in bezug auf die Verteilung von Wirbeln, Schleifen und Bogen und auch von einigen Sondermustern auf den Fingerbeeren gezeigt, daß die bisherigen Publikationen einen Zusammenhang von Krankheiten mit diesen Dermatoglyphen der Fingerbeeren nicht erwiesen haben. – Nicht widerlegt ist die Arbeit von *H. Blotevogel*, die bei 13 von 30 an *Neurofibromatose* erkrankten Personen Zentraltaschen nachweisen konnte, während sich bei den Gesunden der untersuchten Stammbäume die Zentraltaschen nicht fanden und in einer Normalbevölkerung nur etwa 10% aller Personen solche Zentraltaschen aufweisen. Weitere Untersuchungen müssen erweisen, ob tatsächlich eine Korrelation zwischen diesem Muster und der Erkrankung besteht. – Eine weitere Ausnahme zu *Wendts* negativen Ergebnissen bildet die *mongoloide Idiotie*, deren Besonderheiten im Papillarleisten- und Furchungssystem der *Hand* im ersten Teil dieser Arbeit besprochen wurde: An den *Fingerbeeren* fanden sich ausschliesslich ulnare

[1] Herrn Professor Dr. *G. Gerhard Wendt*, Marburg/Lahn, der uns einen Teil des Materials zur Verfügung stellte (siehe auch erste Arbeit, Seite 107), der bei der Aufstellung des Arbeitsprogrammes und bei der Auswertung der Hand und besonders der Finger mitgearbeitet hat, gebührt unser herzlicher Dank, ebenso seiner Mitarbeiterin, Frl. cand. med. *Delingat*.

Schleifen auf allen 10 Fingern in 38% der Mongoloiden gegen 12% einer normalen Kontrollgruppe und radiale Schleifen in 5,7% der Mongoloiden gegen 0,3% bei Normalen. – *Wendt* konnte außerdem eine Beziehung zwischen der Musterverteilung von Wirbeln, Schleifen und Bögen auf den Fingerbeeren und den *Konstitutionstypen* nach *Kretschmer* wahrscheinlich machen, indem Pykniker mehr Wirbel aufweisen als Leptosome und auch sonst einige Unterschiede bei den verschiedenen Typen nachweisbar waren. – Es sei noch erwähnt, daß Krankheitsprozesse die *Dermatoglyphen verwischen* oder auslöschen können, zum Beispiel Lepra, Hornhautvermehrung, Hautatrophie, Pilzinfektion, Narben und Nervenverletzungen.

In bezug auf unser Krankengut (P) und die beiden Kontrollbevölkerungen (Z und M) verweisen wir auf die im ersten Teil dieser Arbeit gemachten Ausführungen.

Für die Untersuchung der Fingerleisten wurden bei den 3 Populationen eine Reihe von Untersuchungen vorgenommen, über deren Ergebnisse im folgenden berichtet wird:

1. Der individuelle Musterwert der Fingerbeeren

Es handelt sich hierbei um eine Zahl, die aus den 10 Fingerbeerenmustern eines Menschen errechnet wird. (Einzelheiten bei *Brodhage und Wendt* [1951] und *Wendt* [1955].) Durchschnitt und Verteilung ergaben keine einwandfreien Unterschiede der Patienten gegenüber den beiden Normalpopulationen.

2. Faktoren V, R, U

Dies sind die von *Bonnevie* angenommenen 3 unabhängigen Gene, die für die Leistenzahl verantwortlich sein sollen und aus der höchsten Leistenzahl auf einem Finger beider Hände, beziehungsweise aus der Differenz zwischen höchsten und geringsten Leistenwerten errechnet werden. – Ein Zahlenvergleich ergibt keinen Unterschied zwischen den 3 Populationen.

3. Sondermuster

Atypische Muster und Störungen traten bei allen 3 Populationen zu selten auf, um einen statistischen Vergleich zu ermöglichen. Jedenfalls waren sie bei den Patienten nicht auffällig häufiger als bei den Vergleichspopulationen. Zentraltaschen und inverse Wirbel waren in Häufigkeit und Verteilung bei den 3 Populationen identisch.

4. Zwischenlinien und weiße Linien

Häufigkeit von Personen mit und ohne diese Muster. Die Zwischenlinien sind schmale, vielfach unterbrochene Linien zwischen den Papillarleisten

ohne Schweißdrüsenmündungen. – Weiße Linien sind gröbere, quer und schräg auf den Fingerbeeren sichtbare Linien, die allem Anschein nach dem sekundären Furchenbild der Hand entsprechen (siehe 1. Teil dieser Arbeit). – In der Häufigkeit der Zwischenlinien und weißen Linien bestand kein Unterschied zwischen den 3 Populationen.

5. *Die Gesamtzahl der Fingerleisten nach Geipel* (= der individuelle quantitative Wert) und die *Gesamtleistenzahl nach Wendt*

Es wird die Gesamtzahl der Leisten aller Finger verzeichnet, wobei Bogen den Wert 0 haben (keine Triradien!), Schleifen *einen* Wert (vom

Tabelle 1

Fingerbeeren: Personen mit und ohne Übergangsformen

	Beobachtungswert	Erwartungswert	χ^2	Beobachtungswert	Erwartungswert	χ^2	
	Patienten (P)			Marburg (M)			P+M
Übergangsform	186	173,68	0,87	360	372,32	0,41	546
Reine Form	100	112,29	1,34	253	240,71	0,63	353
	286	31,81		613	68,19		899
	$\chi^2_{(1)} = 3{,}25$			$p = 0{,}07$			
	Patienten (P)			Zwillinge (Z)			P+Z
Übergangsform	186	179,73	0,23	110	116,27	0,34	296
Reine Form	100	106,26	0,37	75	68,74	0,57	175
	286	60,72		185	39,28		471
	$\chi^2_{(1)} = 1{,}51$			$p = 0{,}2$			
	Zwillinge (Z)			Marburg (M)			Z+M
Übergangsform	110	108,95	∅	360	361,05	∅	470
Reine Form	75	76,03	∅	213	251,97	∅	328
	185	23,18		613	76,82		798
			$\chi^2_{(1)} = 0$				
	Patienten (P)			Marburg + Zwillinge (M+Z)			P+M+Z
Übergangsform	186	173,05	0,98	470	482,95	0,35	656
Reine Form	100	112,91	1,48	328	315,09	0,54	428
	286	26,38		798	73,62		1084
	$\chi^2_{(1)} = 3{,}35$			$p = 0{,}06$			

Triradius zum inneren Terminus), Wirbel 2 Werte (von beiden Triradien zum inneren Terminus). Von diesen beiden Leistenwerten der Wirbel wird bei *Geipel* nur der größere, bei *Wendt* auch der kleinere Wert für die Gesamtzahl verwertet. – Die Patienten unterscheiden sich in bezug auf diese Werte nicht eindeutig von den beiden Normalpopulationen.

6. Die 10 Typen des individuellen Musterwertes und die Fingerhäufigkeit der vorstehenden 10 Typen

Bei dieser Einteilung werden außer den Hauptmustern Bogen (B) und Tannenbogen (T), Schleifen (S), monozentrische Wirbel (W) und doppelzentrische Wirbel (DW) auch die Übergangsformen erfaßt. Die beiden Übergangsformen zwischen B und S sind in einer vergleichenden Statistik wegen ihrer Seltenheit nicht interessant; wohl aber die Übergangsformen zwischen S und W:

SW und DSW: Schleifen mit Übergang zum monozentrischen Wirbel (Sw) oder zum doppelzentrischen Wirbel (DSw), jedoch ohne die Möglichkeit an einer zweiten Seite zu zählen. Hierher gehören auch die Muschelschleifen.

Ws und DWs: Wirbel mit Übergang zur Schleife: monozentrischer Wirbel (Ws) und doppelzentrischer Wirbel oder Doppelschleife (DWs); diese Muster aber nur, wenn der quantitative Wert einer Fingerseite weniger als die Hälfte des Wertes der anderen Seite beträgt.

Verzeichnet man in den 3 Populationen die Häufigkeit dieser 10 Mustertypen, so sind Unterschiede bei diesen Übergangsformen auffällig (Tab. 1). Bei einem Vergleich von Personen mit und ohne Übergangsformen zeigt sich:

a) Patienten (P) gegen die Marburger Vergleichsbevölkerung (M) ergibt mit einem p = 0,07 nur einen statistischen Hinweis;

b) P gegen Zwillinge (Z) mit einem p = 0,2 keinen statistischen Unterschied;

c) da die beiden Normalbevölkerungen (Z gegen M) sich als identisch erweisen, wurde noch P gegen Z + M geprüft, das mit einem p = 0,06 an der Grenze statistischer Sicherung gelegen ist.

Da sich P von Z und von M in der gleichen Richtung dadurch unterschieden, daß *P mehr Personen mit Übergangsformen* aufweist, so soll trotz fehlender statistischer Sicherung diese Beobachtung als ein Hinweis verzeichnet werden.

Wird nun auf jedem einzelnen Finger die Häufigkeit der 10 Mustertypen verzeichnet und die Werte in den 3 Populationen verglichen, so sind bei der großen Zahl von Werten rein zufällig eine Reihe von Unterschieden zu

erwarten, deren tatsächliche Bedeutung nur mit großer Kritik verwertet werden kann. Zunächst sind die beiden Normalpopulationen sehr verschieden und zeigen auf fast allen Fingern Abweichungen voneinander. Es können natürlich nur solche Abweichungen Verwendung finden – und auch diese mit Vorsicht –, in denen P von Z und M in gleicher Richtung abweichen. Dies ist nur bei den oben beschriebenen Übergangsformen der Fall.

Untersucht man auf jedem einzelnen Finger das Verhältnis von Übergangsformen zu reinen Formen, so zeigen die Patienten im Vergleich zu Z und M mehr Übergangsformen auf Finger R II, L II und L III.

Tabelle 2

Fingerbeeren: Übergangsformen (S_W, D_{SW}, W_S, DW_S) gegen reine Formen (S, W, DW)

	Beobachtungswert	Erwartungswert	χ^2	Beobachtungswert	Erwartungswert	χ^2	
R II							
	Patienten (P)			Zwillinge (Z)			P+Z
Übergangsform	40	32,47	1,75	16	23,54	2,41	56
Reine Form	182	189,63	0,31	145	137,47	0,41	327
	222	57,99		161	42,04		383
	$\chi_1^2 = 4{,}88$			$p = 0{,}03$			
L II							
	Patienten (P)			Zwillinge (Z)			P+Z
Übergangsform	36	29,67	1,35	15	21,33	1,88	51
Reine Form	188	194,32	0,21	146	139,68	0,29	334
	224	58,18		161	41,82		385
	$\chi_1^2 = 3{,}73$			$p = 0{,}05$			
L III							
	Patienten (P)			Zwillinge (Z)			P+Z
Übergangsform	27	20,06	2,45	7	13,94	3,50	34
Reine Form	222	228,92	0,21	166	159,08	0,31	388
	249	59,00		173	41,00		422
	$\chi_1^2 = 6{,}47$			$p = 0{,}01$			

	Tabelle II P/Z	Tabelle III P/M	Tabelle IV M/Z
R II	$p = 0{,}03$	$p = 0{,}10$	$p = 0{,}3$
L II	$p = 0{,}05$	$p = 0{,}14$	$p = 0{,}3$
L III	$p = 0{,}01$	$p = 0{,}05$	$p = 0{,}18$

Die statistische Sicherung ist also nicht vorhanden. Immerhin ist der Hinweis erlaubt, daß die oben bereits verzeichnete größere Häufigkeit der Übergangsformen bei P sich vor allem auf R II, L II und L III zu manifestieren scheint.

Tabelle 3

Fingerbeeren: Übergangsformen (S_W, D_{SW}, W_S, DW_S) gegen reine Formen (S, W, DW)

	Beobachtungswert	Erwartungswert	χ^2	Beobachtungswert	Erwartungswert	χ^2	
R II							
	Patienten (P)			Marburg (M)			P+M
Übergangsform	40	32,70	1,63	68	75,29	0,71	108
Reine Form	182	189,25	0,28	443	435,69	0,12	625
	222	30,28		511	69,71		733
		$\chi_1^2 = 2{,}74$		$p = 0{,}1$			
L II							
	Patienten (P)			Marburg (M)			P+M
Übergangsform	36	29,81	1,28	61	67,19	0,57	97
Reine Form	188	194,21	0,20	444	437,79	0,09	632
	224	30,73		505	69,27		729
		$\chi_1^2 = 2{,}14$		$p = 0{,}14$			
L III							
	Patienten (P)			Marburg (M)			P+M
Übergangsform	27	20,25	2,25	37	43,75	1,04	64
Reine Form	222	228,76	0,20	501	494,24	0,09	723
	249	31,64		538	68,36		787
		$\chi_1^2 = 3{,}58$		$p = 0{,}05$			

Diskussion

Eine Beziehung zwischen dem *Finger*leistenmuster und cerebralen Störungen hat sich nicht zeigen lassen, womit die negativen Ergebnisse von *G. G. Wendt* («Fingerleisten und Krankheit»; «Schizophrenie und Fingerleistenmuster») eine weitere Bestätigung und Ergänzung erfahren.

Diese negativen Ergebnisse bestätigen erneut (siehe unsere erste Arbeit Seite 137 138) die von *Degenhardt und Geipel* festgestellte Tatsache, daß Entwicklungsabweichungen sehr wohl an den *Hand*leisten, nicht aber an den später erscheinenden *Finger*leisten entstehen können. Sie sind ein weiterer Hinweis dafür, daß diejenigen Faktoren, die sowohl zur Veränderung der

Tabelle 4

Fingerbeeren: Übergangsformen (S_W, D_{SW}, W_S, DW_S) gegen reine Formen (S, W, DW)

	Beobachtungswert	Erwartungswert	χ^2	Beobachtungswert	Erwartungswert	χ^2	
R II							
	Marburg (M)			Zwillinge (Z)			M+Z
Übergangsform	68	63,87	0,27	16	20,13	0,85	84
Reine Form	443	447,11	0,02	145	140,88	0,01	588
	511	76,04		161	23,96		672
	$\chi_1^2 = 1{,}15$		$p = 0{,}3$				
L II							
	Marburg (M)			Zwillinge (Z)			M+Z
Übergangsform	61	57,63	0,20	15	18,37	0,62	76
Reine Form	444	447,40	0,03	146	142,60	0,08	590
	505	75,83		161	24,17		666
	$\chi_1^2 = 0{,}93$		$p = >0{,}3$				
L III							
	Marburg (M)			Zwillinge (Z)			M+Z
Übergangsform	37	33,29	0,41	7	10,66	1,26	44
Reine Form	501	504,72	0,03	166	161,61	0,12	667
	538	75,67		173	24,33		711
	$\chi_1^2 = 1{,}82$		$p = 0{,}18$				

*Hand*leisten als auch zu cerebralen Störungen geführt haben, im allerfrühesten Embryonalstadium wirksam gewesen sind.

Zusammenfassung

Der Hautleistenvergleich zwischen cerebral geschädigten Kindern und 2 Normalpopulationen ergibt an den *Fingerbeeren* mit den von uns verwandten Untersuchungsmethoden keine statistisch gesicherten Unterschiede.

Es besteht aber eine etwas auffällige, wenn auch statistisch nicht gesicherte, Häufung von Übergangsformen zwischen Schleifen und Wirbeln bei den Patienten, die sich vor allem auf den Fingern R II, L II und L III zu manifestieren scheinen.

Summary

An examination of the dermal ridge-pattern of fingers in children with brain injuries has shown no significant differences from the findings in two control groups. An increased frequency of patterns intermediate between loops and whorls was found in the group of patients, primarily on the second finger of both hands and the third left finger; when compared with the control groups this increase was, however, not significant.

Résumé

La comparaison entre les empreintes digitales chez des enfants présentant des lésions cérébrales et deux populations normales, faites au bout du doigt selon la méthode employée par l'auteur, n'a pas montré de différence significative du point de vue statistique. Toutefois il y a une fréquence frappante, bien que pas statistiquement significative, des formes de transition entre les anses et les tourbillons chez les malades qui semblent se manifester avant tout aux doigts II des deux côtés et au doigt III du côté gauche.

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THE STATISTICAL ANALYSIS OF GENETIC LINKAGE DATA

By G. B. OAKLAND

In all studies of inheritance, questions of gene frequencies and of interrelations of genetic factors are obviously of great importance. For the geneticist who is primarily interested in plants, insects or animals, there is the possibility of experimental breeding of suitable material in such a way as to obtain maximum information in a short time. The student of human genetics is in a much more difficult situation since he is obliged to rely on pedigree records that he or others have collected, often at very considerable trouble and expense. It is therefore important for him to be able to extract from limited and heterogeneous records the greatest possible amount of information on any particular question that interests him.

The discovery of genetic linkages between common hereditary factors or between a common factor and a genetically determined rare disease will add much to the knowledge of the laws of human inheritance. The purpose of this investigation is to develop general methods of procedure for detecting the deviation of a recombination fraction, χ, between any two loci, from the value 0.5. The method consists of assigning to each family in the records a score which will summarize the evidence on that family such that the sum of all scores can be tested for significance by means of its standard error. The formulae for the scores and other functions required depend upon the nature of the allelic genes at each locus and also upon the relations between and phenotypic classifications of the members of the family. Attention will be restricted to family records consisting of mothers and fathers and a number of children for all of whom phenotypes have been fully recorded.

Historical introduction

Bernstein (1931) used for a linkage score, y, a product based on classes of children whose expectation was a function of the recombination fraction averaged over the linkage phases. This enabled the investigator to study linkage in data from only two generations. *Wiener* (1932) introduced another method of detecting linkage and in his work rejected children whose phenotypes gave no information on linkage. Bernstein's methods were improved by *Hogben* (1934) and *Haldane* (1934, a, b).

Any function of χ whose expectation is zero could be used as a test function in detecting linkage. What is required is some criterion for choosing a function to get the best out of the data. *Fisher* has shown that scores based on the principle of maximum likelihood have an optimal property of being at least as efficient as any alternative method. No alternative method can give a score whose standard error is smaller.

To show deviation from the null hypothesis of independent inheritance, *Fisher* (1935, a, b, 1936) introduced the u-statistics: u_{11}, u_{31}, u_{33}, as efficient scores applicable to families consisting of two or more children for some of the simpler cases of mating. With independent inheritance, the expected value of the score is zero; with linkage, its expected value is positive. These u-statistics were applied to family records in which dominant and recessive abnormalities occurred and were shown to be more efficient than *Bernstein's* y-statistic. The ratio of the efficiency of y to that of u was 77 per cent for loose linkage, falling gradually to 72 per cent for close linkage.

The u-score technique introduced by *Fisher* was developed further by *Finney*. In a series of papers (1940, 1941, a, 1941, b, 1942, a, 1942, b, 1942, c, 1943), *Finney* developed the scoring procedure for a wide variety of mating types. He discussed the necessity for using the evidence of phenotypes of children for determining the parental genotypes so as to ascertain whether a family could give information on linkage. He showed that matings involving the ABO blood group system with three allelomorphic genes could be scored by means of his tables. *Finney* (1941, b) extended his results to incomplete parental testing where the known frequencies of marker genes are used to score families whose genotype with respect to one factor was uncertain.

Penrose (1935) based his test of linkage on records of brothers and sisters alone, using the fact that linkage will tend to increase the frequency of some types of sib-pairs relative to others. In the first instance he dealt with characters on a continuous scale and in (1938) he extended his method to describe a discrete classification. By using a three-fold classification of sib-

pairs for each factor he increased the efficiency of his sib-pair method (1946). Later papers (1946, 1950, 1951, 1953) dealt with improvements in his method and showed how to examine sib-pair material for linkage between the locus of a gene determining red hair and the ABO locus.

The simplicity of the computation of *Penrose's* methods made them attractive to investigators who had records of parents as well as of children. *Finney* pointed out that the adoption of *Penrose's* technique when parental records were available frequently involved loss of efficiency.

Haldane (1946) showed that the assumption of normality may be misleading for cases where the data are on the borderline of significance. A correction for skewness was derived for cases where the score is less than three times its standard error.

Haldane and Smith (1947) proposed backward odds as a test for linkage and took for the test ratio, a ratio of two posterior probabilities; one calculated on the basis of the null hypothesis, the other on an alternative hypothesis. *Smith* (1953) lists ten steps for the calculation of backward odds (or lods when common logarithms of odds are taken). The calculation for many families is laborious and the process is better suited for electronic computation when extensive data are to be used.

Smith (1954) pointed out that, since examples are known in animal genetics where there is a sex different in the values of χ, the use of separate scores may show a sex difference in man. His scores are based on the probabilities of a child receiving genes of the test factor from the mother or from the father. The addition of his scores for the mother and the father provides the score without the separation of the sexes and formulae are given for the variance of the combined score. When genotypes are unknown gene frequencies in the population may be used but the above technique is laborious when many mating types are encountered.

Bailey (1951, a) gave a general development of u-statistics and a simplified approach to the computation of scores, score corrections and amounts of information for *Finney's* mating types. *Bailey's* method is essentially the same as *Finney's* but provides a more concise and systematic method of dealing with new mating types and very much simplifies the algebraic analysis. This was extended (1951, b) to estimate the penetrance in addition to the recombination fraction. A more detailed discussion of *Bailey's* techniques is given below.

Mohr (1954) analysed, by means of *Finney's* and *Penrose's* techniques, extensive data for the study of linkage between many marker genes and between marker genes and other traits.

A further use of the score of the *Fisher-Finney-Bailey*-type is that the

observed value of the total score gives an estimate of the recombination fraction. This estimate is not fully efficient but except for close linkage the estimate based on this score is highly efficient.

Mathematical approach

Fisher applied the method of maximum likelihood (*Finney*, 1948) to obtain a more efficient score. All such scores are quadratic functions of the frequency of different phenotypes. The application of an appropriate differential operator to a multinomial generating function for a family of size s will lead to an evaluation of the expectation of the score. This expectation is given as a multiple of

$$1\text{–}4\,\xi \quad \text{where}$$
$$\xi = \chi(1-\chi)$$

and χ is the recombination fraction. The score was then used to give an estimate of $1\text{–}4\,\xi$ with an appropriate divisor. Under the null hypothesis of no linkage, the sampling variance of the score was evaluated. *Finney* (1940) showed that the divisor of the score, its sampling variance and the amount of information could be made identical for any type of mating by a proper choice of score and units. In *Finney's* notation, $\varkappa$ represents both the variance of the score, λ, and the quantity of information with respect to $1\text{–}4\,\xi$ as well as the total information available from the operation. Tables of mating types with appropriate scores and amounts of information were given. The appropriate score was essentially a multiple of one of three u-statistics introduced by *Fisher*:

$$u_{11} = (a-b-c+d)^2-(a+b+c+d)$$
$$u_{31} = (a-3b-c+3d)^2-(a+9b+c+9d)$$
$$u_{33} = (a-3b-3c+9d)^2-(a+9b+9c+81d)$$

where a, b, c, d are numbers of children in classes of phenotypes. *Finney* showed that, for some of the more complex mating types in which, despite dominance, the parental genotype can be determined from the occurrence of particular phenotypes in the children. These families, *Finney* designates as "certain". Associated with the scores of these families are score corrections. These are also given in his tables. Parts of table 1 (*Finney*, 1940) and table 1 (*Finney*, 1941, a) are reproduced here as tables 1 and 2 for reference.

Finney assessed the efficiency of other methods of scoring by comparison of the information extracted by their methods with that for the maximum

Table 1

Table of scoring systems

Type	Mating	a	b	c	d	λ	$\bar{\lambda}$	I
1	td × TD	TD	tD	Td	td	$^1/_2u_{11}$		ω_1
2	Td × TD	TD	tD	Td	td	$^1/_{18}u_{31}$		ω_2
3	Md × MND	MD	MND	Md	MNd	$^1/_2u_{11}$		ω_1
4	MNd × MND	MD	ND	Md	Nd	$^1/_2u_{11}$		ω_1
13	tw × TW	TW	tW	Tw	tw	$^1/_2u_{11}$	ε_5	ω_5
14	Tw × TW	TW	tW	Tw	tw	$^1/_{18}u_{31}$	ε_6	ω_6
15	TW × TW	TW	tW	Tw	tw	$^1/_{81}u_{33}$	ε_7	ω_1
16	Mw × MNW	MW	Mw	MNW	MNw	$^1/_2u_{11}$		ω_1
17	MNw × MNW	MW	Mw	NW	Nw	$^1/_2u_{11}$		ω_1
18	MW × MNW	MW	Mw	MNW	MNw	$^1/_{18}u_{31}$		ω_2
19	MNW × MNW	MW	Mw	NW	Nw	$^1/_9u_{31}$		$4\ \omega_2$
20	MP × MNPQ	MPQ	MNPQ	MP	MNP	$^1/_2u_{11}$		ω_1
21	MNP × MNPQ	MPQ	NPQ	MP	NP	$^1/_2u_{11}$		ω_1
22	MNPQ × MNPQ	MP	NP	MQ	NQ	u_{11}		$4\ \omega_1$

Table 2

Table of scoring systems for ABO matings

Type	Mating	a	b	c	d	λ	$\bar{\lambda}$	I
1	ABd × AD	ABD	BD	ABd	Bd	$^1/_2u_{11}$	–	ω_1
3	Ad × ABD	AD	BD ABD	Ad	Bd AB	$^1/_2u_{11}$	–	ω_1
13	ABt × AT	ABT	BT	ABt	Bt	$^1/_2u_{11}$	ε_5	ω_5
16	At × ABT	AT	BT ABT	At	Bt ABt	$^1/_2u_{11}$	–	ω_1
18	ABT × AT (1)	AT	At	BT ABT	Bt ABt	$^1/_{18}u_{31}$	–	ω_2
14	ABT × AT (2)	ABT	ABt	BT	Bt	$^1/_{18}u_{31}$	ε_6	ω_6
16	ABM × AMN	ABMN	BMN	ABM	BM	$^1/_2u_{11}$	–	ω_1
20	AM × ABMN	AMN	BMN ABMN	AM	BM ABM	$^1/_2u_{11}$	–	ω_1
21	ABMN × AMN (1)	AM	AN	BM ABM	BN ABN	$^1/_2u_{11}$	–	ω_1
	ABMN × AMN (2)	ABM	ABN	BM	BN	$^1/_2u_{11}$	–	ω_1

likelihood estimate. *Finney* found (1941, b) in a heterogeneous collection of 200 families in which sib-pairs had been used that to obtain a test of linkage as precise as that of efficient scores based on 200 families, the method of sib-pairs would require 1000 families. *Fisher* had shown earlier (1935, a) that for the efficiency of estimation of linkage "save for close linkage, the equation based on u is rather highly efficient. For very close linkage the efficiency tends to zero.... For detection it is the efficiency at 50 per cent recombination which measures the sensitiveness of the method." Thus the u-statistics are fully efficient scores for the detection of linkage and estimates of the recombination fraction based on them in the neighbourhood of $\chi = .5$ are highly efficient.

Although, as *Haldane* (1946) has emphasized that the distribution of scores is not strictly normal, the effect of skewness will not be serious provided the total information does not come mostly from a few large families. When the records consist of a large number of families, the u-statistics can be used quite safely as long as the investigator bears in mind the above proviso.

This paper considers only families ascertained through the parents. Thus, a sample of families is taken, the phenotypes of the parents determined and the families chosen for the records are those for which the genotypes of the parents are "certain". The genotypes of parents are not necessarily determined by direct test of the parents themselves and it is permissible to include families where the heterozygous character of one or both parents is shown by additional information from children of the mating or other blood relatives. The general method of deriving u-statistics and their corresponding amounts of information follows the simplified method given by *Bailey* (1951, a, b).

All equations involving the probability generating functions and total frequency are considered to be written down with respect to one of the phases. Because of an averaging operation for the phases under consideration: both parents in coupling, both parents in repulsion, or one parent in coupling, the other in repulsion, the formulae for the scores and their information hold for all phases.

The probabilities, f_i, of distinguishable families of size s are given by the coefficients of $\pi \propto_i^{a_i}$ in the probability generating function:

$$\Phi = \left(\sum_{i=1}^{16} \propto_i f_i\right)^s = (1, 2, 3, \ldots 15, 16)^s$$

with the total frequency $F = \Sigma f_i = 1$ and $\Sigma a_i = s$ of admissible families.

The expression $(1, 2, 3, \ldots 15, 16)^s$ will be used as a simplified notation for the multinomial above.

It will sometimes be convenient to write the two recombination fractions, χ_1 und χ_2, as though they were not equal. This will enable us to differentiate the probability, f_i, with respect to χ_1 and χ_2 separately.

By the maximum likelihood method *Bailey* (1951, a) derives an expression for the generalized u-statistics. The expression for the score in formula 11 (1951, a) becomes:

$$\lambda = c_i\, u \left(\frac{\bar{f}'}{\bar{f}}\right) \tag{1}$$

$$\left.\begin{aligned} \lambda_1 &= c_i\, u \left(\frac{\bar{f}_1'}{\bar{f}_1}\right) \\ \lambda_2 &= c_i\, u \left(\frac{\bar{f}_2'}{\bar{f}_2}\right) \end{aligned}\right| \qquad (1)'$$

By means of a differential operator, he found the amounts of information:

$$\mathrm{I} = 2c_i^2\, s\, (s-1) \left(\sum \frac{\bar{f}'^{\,2}}{\bar{f}}\right)^2 \tag{2}$$

$$\left.\begin{aligned} \mathrm{I}_1 &= 2c_i^2\, s\, (s-1) \left(\sum \frac{\bar{f}'^{\,2}}{\bar{f}_1}\right)^2 \\ \mathrm{I}_2 &= 2c_i^2\, s\, (s-1) \left(\sum \frac{\bar{f}_2'^{\,2}}{\bar{f}_2}\right)^2 \end{aligned}\right| \qquad (2)'$$

Where the generalized u-statistic:

$$\mu \left(\frac{\bar{f}'}{\bar{f}}\right) = \left(\sum \frac{\bar{f}'}{\bar{f}}\, a_i\right)^2 - \sum \left(\frac{\bar{f}'}{\bar{f}}\right)^2 a_i$$

and f_i are the probabilities of the phenotypes, $\bar{f}_i$ their values if no linkage exists and $\bar{f}_1'$, $\bar{f}_2'$ the derivatives of f_i with respect to χ_1 and χ_2 respectively.

The table below gives the values of c_i for different situations:

	c_i	equations used for λ and I
1. Linear function of χ	$^1/_8$	(1), (2)
2. Linear function of θ	$^1/_{16}$	(1), (2)
(θ being χ^2, $(1-\chi)\,\chi$ or $(1-\chi)^2$)		

	c_i	equations used for λ and I
3. Symmetrical in χ_1 and χ_2	$^1/_4$	(1), (2) but differentiate with respect to only one, say χ_1
4. Non-symmetrical in χ_1 and χ_2	$^1/_8$	$(1)'$, $(2)'$

When either or both factors show dominance, the above equations for scoring and amount of information do not apply. The appropriate probability-generating function, Φ, then contains corrective terms because of the rejection of doubtful families. For example, it may be necessary to reject families in which children are of p phenotypes:

$$\Phi_1 = \left(\sum_1^n \propto_i f_i\right)^s - \left(\sum_1^p \propto_i f_i\right)^s, \; n > p$$

Again it may be necessary to reject families in which neither one set of n—p nor another set of n—p phenotypes are represented so giving the generating function:

$$\Phi_2 = \left(\sum^n \propto_i f_i\right)^s - \left(\sum^p \propto_i f_i\right)^s - \left(\sum^q \propto_i f_i\right)^s + \left(\sum^r \propto_i f_i\right)^s$$

$$\text{where } \; n > p, \quad n > q, \quad n > r.$$

Equations similar to (1) and (2) for evaluating the score and the amount of information are:

$$\lambda = c_i \, \mu \left(\frac{f'}{\overline{f}}\right) - \overline{\lambda} \tag{3}$$

$$\text{with the score correction, } \overline{\lambda} = c_i \frac{\overline{F}''}{\overline{F}}$$

and $\overline{F}$ = frequency of admissible families,

$$\text{and } I = c_i^2 \left(\frac{(D\overline{\Phi})''}{\overline{F}}\right) - \overline{\lambda}^2 \tag{4}$$

Whenever it is necessary to evaluate the χ_1 and χ_2 effects separately, equations similar to $(1)'$ and $(2)'$ are available:

$$\lambda_i = c_i \, \mu \left(\frac{\overline{f'_i}}{\overline{f}}\right) - \overline{\lambda}_i$$

$$\text{where } \overline{\lambda}_i = c_i \frac{\overline{F}_i''}{\overline{F}}$$

$$\text{and } I_i = c^2 \left(\frac{(D\Phi_i)''}{\overline{F}}\right) - \overline{\lambda}^2{}_i$$

$$i = 1, 2.$$

The subscript i = 1,2 indicates differentiation with respect to χ_1 and χ_2 respectively and c takes the values given in the above table.

The unprimed equations are used when we are concerned with only coupling or repulsion. The primed equations are used when the two parents may both be in coupling or one in coupling and one in repulsion or both in repulsion.

After performing the indicated differentiation in the equations immediately above, we have on simplification:

$$\overline{\lambda}_i = c \frac{\overline{F}_i'}{\overline{F}} = \frac{c\, s\,(s-1)}{\overline{F}} \left[(\Sigma \bar{f}_i)^{s-2} (\Sigma \bar{f}'_i)^2 \ldots\right] \tag{3$'$}$$

and

$$I_i = c^2 s\,(s-1) \left[\begin{array}{l} 2\,(\Sigma \bar{f}_i)^{s-2} \left(\Sigma \dfrac{\bar{f}_i'^2}{\bar{f}}\right)^2 + 4\,(s-2)\,(\Sigma \bar{f}_i)^{s-3}\,(\Sigma \bar{f}'_i)^2 \\ \left(\dfrac{\Sigma \bar{f}'^2}{\bar{f}}\right) + (s-2)\,(s-3)\,(\Sigma \bar{f}'_i)^4\,(\Sigma \bar{f}_i)^{s-4} \ldots \end{array}\right]$$

where the square bracket contains terms of similar form for each component of the generating function. Whenever $(\Sigma f')$ is zero, the score correction factor, $\overline{\lambda}$, becomes zero and the formula for I_i simplifies. The above two expressions hold for equations (3) and (4) also.

As an example consider the mating:

$$A_1 A_2\, B_1 B_2 \times A_1 B_1 B_2$$

where the A factor consists of two genes each dominant to a third gene but showing no dominance to each other and the two allelomorphic genes of the B factor show no dominance.

If there exists an A_2 child, then the above mating is doubly heterozygous in both factors for both parents and is:

$$A_1 A_2 B_1 B_2 = A_1 A_3 B_1 B_2$$

The following phenotypes from the mating are possible:

A_1B_1	–	–	–
$A_1A_2B_1$	A_2B_1	–	–
$A_1B_1B_2$	–	A_1B_2	–
$A_1A_2B_1B_2$	$A_2B_1B_2$	$A_1A_2B_2$	A_2B_2

and have for their probabilities in coupling:

$$
\begin{array}{cccc}
\dfrac{1-\chi_1}{4} & - & - & - \\[2ex]
\dfrac{\chi_1(1-\chi_2)}{4} & \dfrac{\chi_1\chi_2}{4} & - & - \\[2ex]
{}^1/_4 & - & \dfrac{\chi_1}{4} & - \\[2ex]
\dfrac{1-\chi_1-\chi_2+2\chi_1\chi_2}{4} & \dfrac{\chi_1+\chi_2-2\chi_1\chi_2}{4} & \dfrac{(1-\chi_1)\,\chi_2}{4} & \dfrac{(1-\chi_1)\,(1-\chi_2)}{4}
\end{array}
$$

Since the phenotype $A_1B_1B_2$ has a probability of ${}^1/_4$ it contributes nothing to the detection of linkage, and will be rejected. That is to say the scoring will be based on the conditional probability for families having s children exclusive of any of these phenotypes. The derivatives $\bar{f}_1'$, $\bar{f}_2'$, of the probabilities of the phenotypes, $A_1A_2B_1B_2$ and $A_2B_1B_2$, are zero and so they also make no contribution to the detection of linkage and will be rejected. The frequency of such children might be used in any efficient estimate of the recombination fraction whereas obviously the frequency of A_1A_2 is irrelevant even for this purpose. Hence for the detection of linkage, the frequencies of these three phenotypes are rejected and a probability generating function based on a reduced family size is constructed.

The probabilities, f_i, conditional on this rejection are:

$$
\begin{array}{cccc}
\dfrac{1-\chi_1}{2} & - & - & - \\[2ex]
\dfrac{\chi_1(1-\chi_2)}{2} & \dfrac{\chi_1\chi_2}{2} & \cdot & \\[2ex]
- & - & \dfrac{\chi_1}{2} & - \\[2ex]
- & - & \dfrac{(1-\chi_1)\,\chi_2}{2} & \dfrac{(1-\chi_1)\,(1-\chi_2)}{2}
\end{array}
$$

In scoring for χ_1, the basic quantities are:

$$
\begin{array}{cccc}
\bar{f}_1 & \bar{f}_1' & \dfrac{\bar{f}_1'}{\bar{f}_1} & \dfrac{\bar{f}_1'^2}{\bar{f}_1} \\[2ex]
\begin{array}{cccc} {}^1/_4 & \cdot & \cdot & \cdot \\ {}^1/_8 & {}^1/_8 & \cdot & \cdot \\ \cdot & \cdot & {}^1/_4 & \cdot \\ \cdot & \cdot & {}^1/_8 & {}^1/_8 \end{array} &
\begin{array}{cccc} -{}^1/_2 & \cdot & \cdot & \cdot \\ {}^1/_4 & {}^1/_4 & \cdot & \cdot \\ \cdot & \cdot & {}^1/_2 & \cdot \\ \cdot & \cdot & -{}^1/_4 & -{}^1/_4 \end{array} &
\begin{array}{cccc} -2 & \cdot & \cdot & \cdot \\ 2 & 2 & \cdot & \cdot \\ \cdot & \cdot & 2 & \cdot \\ \cdot & \cdot & -2 & -2 \end{array} &
\begin{array}{cccc} 1 & \cdot & \cdot & \cdot \\ {}^1/_2 & {}^1/_2 & \cdot & \cdot \\ \cdot & \cdot & 1 & \cdot \\ \cdot & \cdot & {}^1/_2 & {}^1/_2 \end{array}
\end{array}
$$

Bailey's simplified approach gives:

$$\Phi_1 = (1, 2, 3, 4, 5, 6)^s - (1, 2, 4, 5)^s,$$

families represented by $(1, 2, 4, 5)^s$ are rejected since by themselves they would not ensure the heterozygosity of the A factor in the second parent. Only phenotypes A_2 in combinations with the other phenotypes ensure the certainty of the second parent.

The following notation is useful. Write the observed frequencies to conform with the six phenotypes above.

$$\begin{array}{cccc} a_1 & - & - & - \\ a_2 & a_3 & - & - \\ - & - & a_4 & - \\ - & - & a_5 & a_6 \end{array}$$

When the notation

$$\left|\begin{array}{cccc} -2 & - & - & - \\ 2 & 2 & - & - \\ - & - & 2 & - \\ - & - & -2 & -2 \end{array}\right|$$

is used, multiply each of the numbers between the vincula and brackets by the corresponding observed frequency, a_i, cell by cell and add the products.

$c_1 = {}^1/_8,$

$$\lambda_1 = {}^1/_8 \left\{ \left[\begin{array}{cccc} -2 & - & - & - \\ 2 & 2 & - & - \\ - & - & 2 & - \\ - & - & -2 & -2 \end{array}\right]^2 - \left|\begin{array}{cccc} 4 & - & - & - \\ 4 & 4 & - & - \\ - & - & 4 & - \\ - & - & 4 & 4 \end{array}\right| \right\} = {}^1/_2 u_{11}$$

$$\bar{F}_1 = \frac{4^s - 3^s}{4^s}$$

$$\bar{\lambda}_1 = {}^1/_8 \, \frac{s\,(s-1)}{\bar{F}_1} \, [1.0 - ({}^3/_4)^{s-2} \, .0] = 0.$$

$$I_1 = {}^1/_8{}^2 \, \frac{s\,(s-1)}{4^s - 3^s} \, [2.1.4^2 - 2\,({}^3/_4)^{s-2}\, 3^2]\, 4^s$$

or $I_1 = {}^1/_2 s(s-1) = \omega_1$.

Again in scoring for χ_2, the probabilities: $\frac{1-\chi_1}{2}, \frac{\chi_1}{2}$ of phenotypes, A_1B_1

and $A_1 B_2$ are not functions of χ_2 and provide no information for the detection of linkage of χ_2. Hence children $A_1 B_1$ and $A_1 B_2$ are rejected; thus all A_1 and all $B_1 B_2$ children have been rejected and the conditional probabilities, f_2, now are:

–	–	·	–
$\chi_1 (1-\chi_2)$	$\chi_1 \chi_2$	–	–
–	–		–
–	–	$(1-\chi_1)\, \chi_2$	$(1-\chi_1)\,(1-\chi_2)$

and shall be written as below with the necessary basic quantities for scoring χ_2.

f_2	$\bar{f}_2$	$\bar{f}'_2$	$\dfrac{\bar{f}'_2}{\bar{f}_2}$	$\dfrac{\bar{f}'^2_2}{\bar{f}_2}$
$\chi_1(1-\chi_2)$	$^1/_4$	$-^1/_2$	-2	1
$\chi_1\chi_2$	$^1/_4$	$^1/_2$	2	1
$(1-\chi_1)$	$^1/_4$	$^1/_2$	2	1
$(1-\chi_1)\,(1-\chi_2)$	$^1/_4$	$-^1/_2$	-2	1

$$c_{_1} = {}^1/_8$$

$$\lambda_2 = {}^1/_8 \left\{ \overline{\begin{matrix} -2 \\ 2 \\ 2 \\ -2 \end{matrix}}^{\,2} - \overline{\begin{matrix} 4 \\ 4 \\ 4 \\ 4 \end{matrix}} \right\} = {}^1/_2 u_{11}$$

$$\bar{F}_2 = \frac{2^s - 1}{2^s}$$

$$\bar{\lambda}_2 = {}^1/_8 \; \frac{s\,(s-1)}{\bar{F}_2} \,[1.0 - ({}^1/_2)^{s-2}\, 0] = 0$$

$$I_2 = {}^1/_8{}^2 \; \frac{s\,(s-1)}{(2^s - 1)} \,[2.1.4^2 - 2.\, ({}^1/_2)^{s-2}\, 2^2]\; 2s$$

or $I_2 = {}^1/_2 s\,(s-1) = \omega_1$.

Three procedures

When the mating is certain for both parents, it is sometimes convenient to write down the probabilities as though the recombination fractions for the two parents are not necessarily equal. Various examples are known from animal genetics where the recombination fractions are not the same for males and females. *Fisher* (1953) showed, in the linkage of Polydactyly with Leaden in the house mouse, the recombination fraction for females to

be larger than that for males. It will be found in many cases that, when the contributions of the parents are listed separately, the computation of scores and amounts of information are simplified. Three procedures are then possible:

(1.) If it is assumed that the recombination fractions for the two parents have a common value, χ, then scores, score correction factors and amounts of information are calculated for each family in the record if both parents are heterozygous in each factor. Some matings yield a score which is the sum of two u-statistics, corresponding to the separate contributions of the parents. It is then convenient to list the scores, score correction factors and the appropriate amounts of information separately. When the assumption, $\chi_1 = \chi_2$, is made, the two scores are added and the two amounts of information are added giving one score and its corresponding amount of information.

This is the technique used in *Bailey*'s simplified method as seen from p. 41 of *Bailey* (1951, b). "*Finney*'s recommendation that, for practical purposes, we ignore the small correlations between the two parts of the score and use the appropriate amounts of information attachable to the parts separately, can be extended to the present case.". If only one parent is doubly heterozygous the family may still be scored in this procedure.

Whenever the probabilities are linear in χ or θ, procedure 1 is straightforward. If the probabilities are non-linear in χ or θ but symmetrical in χ_1 and χ_2 then calculation of the basic quantities used in *Bailey*'s simplified approach is made by differentiating with respect to one, say, χ_1, and the constant $c = 1/4$. When the probabilities are neither linear in χ or θ nor symmetrical in χ_1 and χ_2, procedure 1 is illustrated below. Using procedure 1, on the ABO mating, ABT $\times$ AT, in table 1 (*Finney*, 1941), the basic quantities are:

	Phenotype	f_1	$\bar{f}_1$
1.	AT	$\frac{2 - \chi_1}{4}$	$6/16$
2.	ABT	$\frac{1 - \chi_2 + \chi_1 \chi_2}{4}$	$3/16$
3.	BT	$\frac{\chi_1 + \chi_2 - \chi_1 \chi_2}{4}$	$3/16$
4.	At	$\frac{\chi_1}{4}$	$2/16$
5.	ABt	$\frac{\chi_2 (1 - \chi_1)}{4}$	$1/16$
6.	Bt	$\frac{(1 - \chi_1)(1 - \chi_2)}{4}$	$1/16$

In scoring for χ_1 combinations of all six phenotypes are used and the generating function, for determining the scoring of χ_1 expressed symbolically, is:

$$\Phi_1 = (1, 2, 3, 4, 5, 6)^6 - (1, 2, 3)^S - (1, 2, 4, 5)^S + (1, 2)^S.$$

Using *Bailey's* simplified method, the values obtained for the score, the score correction factor and the amount of information are:

$$\lambda_1 = {}^1/_{18}\ \mu_{31}$$
$$\bar{\lambda}_1 = {}^1/_2\ \varepsilon_7$$
$$\mathrm{I}_1 = \omega_{101}$$

In scoring for χ_2, phenotypes AT and At are rejected and the basic quantities and the generating function for determining the score of the second parent are:

	Phenotype	f_2	$\bar{f}_2$
1.	ABT	$\frac{1-\chi_2+\chi_1\chi_2}{2}$	$^3/_8$
2.	BT	$\frac{\chi_1+\chi_2-\chi_1\chi_2}{2}$	$^3/_8$
3.	ABt	$\frac{\chi_2(1-\chi_1)}{2}$	$^1/_8$
4.	Bt	$\frac{(1-\chi_1)(1-\chi_2)}{2}$	$^1/_8$

then $\Phi_2 = (1, 2, 3, 4)^S - (1, 2)^S - (1, 3)^S + (1)^S$, with $\lambda_2 = {}^1/_{18}\ \mu_{31}$, $\bar{\lambda}_2 = \varepsilon_6$, $\mathrm{I}_2 = \omega_6$ as given in table 1 of (*Finney* 1941).

The null hypothesis that there is no linkage may be tested and, if contradicted, an estimate of χ may be made from the total score and the quantity of information. Procedure 1 is the procedure followed for the non-dominant and dominant types considered here.

(2.) If it is assumed that the recombination fractions are not necessarily equal, then separate scores and amounts of information may be calculated for one parent independent of the other parent. For example, scores and quantities of information may be calculated for all fathers in the records. If the null hypothesis of no linkage is contradicted, an estimate of χ_1 may be made from the total score and the quantity of information.

(3.) If it is assumed that the recombination fractions are not necessarily equal, it may be desirable to estimate the recombination fraction of one parent conditional on the assumption that the other parent's recombination fraction is $^1/_2$. For example, if the following values were found for the two recombination fractions and their standard errors:

$$\chi_1 = .25 \pm .02$$
$$\chi_2 = .49 \pm .03,$$

a conditional assumption that $\chi_2 = {}^1/_2$ may be made. Then on this conditional assumption, scores and amounts of information are calculated for, say, all fathers for the families in the record. If the null hypothesis is contradicted then an estimate of χ_1 is made conditional on $\chi_2 = {}^1/_2$. Similarly a conditional estimate of χ_2 may be made assuming $\chi_1 = {}^1/_2$ but the two conditional estimates cannot be made simultaneously.

Procedure 2 cannot be used whenever expected frequencies are symmetrical in χ_1 and χ_2 but a conditional estimate of either parent's recombination fraction may be made separately if the null hypothesis is contradicted. Procedures 1 and 3 may be used in any of the mating types which are scorable.

The logical approach in the examination of phenotypes

A score is defined for a family of a particular type of mating and is calculated from the numbers of children of different phenotypes. Initial entry into the tables of scoring systems must be by parental phenotypes.

There are three situations with respect to certainty of the genotypes in the matings:

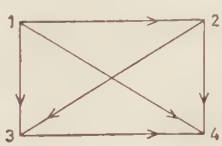
(a) the genotype is known either from

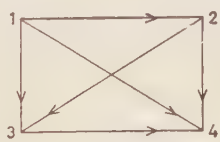
(1) the mating,

(2) auxiliary information,

or (3) the children.

(b) there is a twilight case where the mating is known to be doubly heterozygous in each factor and the scoring is certain but one heterozygote may be of doubtful genotype. Consider by way of example the genetic systems whose dominance relations are specified by arrows between the genes in the diagram below:

A 

 B

The mating: $A_1 \times A_1$, is scorable if there exists an A_2 child. The mating by genotypes could be any one of the following scorable matings:

$$A_1A_2 \times A_1A_2,$$
$$A_1A_2 \times A_1A_3,$$
$$A_1A_2 \times A_1A_4.$$

Thus the second parent is a heterozygote but of doubtful genotype and the mating could then be written:

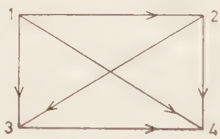
$$A_1A_2 \times A_1 \begin{bmatrix} A_2 \\ A_3 \\ A_4 \end{bmatrix}$$

(c) the genotypes are doubtful.

Where neither factor shows dominance, the genotypes are observable and no further information is needed to enter into the table. If either or both factors show dominance, some phenotypes will leave corresponding genotypes indeterminate. Matings then cannot be scored without additional information.

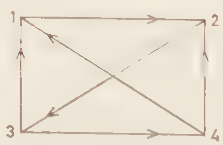
Such additional information may come from an examination of the phenotypes of the blood relations of the parent in question. In human records this is rather unusual as the usual recording is made from the family unit: parents and children. Thus a more fruitful source of such information is the children of the mating.

An illustration of the use of information from blood relatives occurs when the genes of the A factor obey the following dominance relationships:



If in a mating from this system, the father is an A_1 phenotype but has two sibs: A_3 and A_4 phenotypes. Since there exists an A_3 sib, this ensures that A_1 is an A_1A_4 and in turn that A_4 must be a homozygote: A_4A_4. Both his parents must have carried an A_4 gene. Thus A_1 is demonstrated to be a heterozygote, A_1A_4.

When examination of the phenotypes of the children of the mating is made to clarify the uncertainty of the mating, the process may be arranged into five steps. These steps are illustrated by means of the A factor whose genes obey the dominance relations:



and for the mating, $A_3 \times A_4$, in this genetic system.

(1.) The investigator knows his genetic system. He has four genes: A_1, A_2, A_3, A_4. Between each pair he can state what dominance exists.

(2.) He lists the possible inferences in this system from phenotypes to genotypes. For the above example these inferences are:

Phenotype	Represents	Genotypes
A_1		A_1A_1 A_1A_2
A_2		A_2A_2 A_2A_3
A_3		A_3A_3 A_3A_4 A_3A_1
A_4		A_4A_4 A_4A_1 A_4A_2

(3.) He observes a particular pair of parents. If step 2 shows both parents homozygous, he discards the record; otherwise he examines all possible combinations of genotypes of the mating as in step 2 and lists the phenotypes of the children which could arise from such matings.

Obviously a rejection is not made for the mating:

$$A_3 \times A_4.$$

Since both A_3 and A_4 phenotypes each represent three genotypes, any one of the nine matings:

$$\begin{matrix} A_3A_3 & & A_4A_4 \\ A_3A_4 & \times & A_4A_1 \\ A_3A_1 & \times & A_4A_2 \end{matrix}$$

are possible. The phenotypes of the children possible from these nine matings are listed in table 3.

Table 3

Phenotypes of children

		A_1	A_2	A_3	A_4
Parental matings	$A_3A_3 \times A_4A_4$			×	
	$A_3A_3 \times A_4A_1$			×	
	$A_3A_3 \times A_4A_2$		×	×	
	$A_3A_4 \times A_4A_4$			×	×
	$A_3A_4 \times A_4A_1$			×	×
	$A_3A_4 \times A_4A_2$		×	×	×
	$A_3A_1 \times A_4A_4$			×	×
	$A_3A_1 \times A_4A_1$	×		×	×
	$A_3A_1 \times A_4A_2$	×	×	×	×

(4.) He classifies the s children phenotypically. A set of genotypes is listed opposite each child.

If in this family there are 3 children whose phenotypes are A_1, A_2, and A_4, the appropriate genotypes are:

$$\begin{array}{llll} A_1: & A_1A_1 & A_1A_2. & \\ A_2: & A_2A_2 & A_2A_3. & \\ A_4: & A_4A_4 & A_4A_1 & A_4A_2. \end{array}$$

Use is now made of the fact that all the s children have the same individuals as parents. In view of this, some parental genotypes may be excluded. In this example, all genotypes but, $A_3A_1 \times A_4A_2$ are excluded.

(5.) The last step is to use the information found in 4 to list a reduced set of genotypes opposite the phenotypes of the children.

Thus:

$$\begin{array}{l} A_1 \text{ is } A_1A_2 \\ A_2 \text{ is } A_2A_3 \\ A_4 \text{ is } A_4A_1. \end{array}$$

It follows from the discussion and table 3 that the presence of either A_2 or A_4 but not both and not A_1 phenotypes is sufficient to ensure that the mating, $A_3 \times A_4$, is heterozygous for one parent only in this factor. The presence of (A_1 and, or A_2) and A_4 phenotypes is sufficient to ensure that the mating is heterozygous for both parents in this factor.

Scorable family size

In many matings in a genetic system the probabilities of the phenotypes of the children are such functions of χ that each child can contribute something to the detection of linkage, provided that the family size, s, is greater than 1. In some matings, however, the probability of a particular phenotype makes it obvious that such children can not contribute any information to the detection of linkage. Such an example occurs for the mating:

$$A_1A_2B_1B_2 \times A_1A_3B_1B_2.$$

The phenotype $A_1B_1B_2$ had a probability of $1/4$ and was rejected, thus reducing the scorable family size.

In other matings the probabilities of some phenotypes are such functions of χ_1 and χ_2 that these phenotypes are unable to contribute any information to the u-scores. For example a phenotype having a probability, $\frac{\chi_1 + \chi_2 - 2\chi_1\chi_2}{4}$, makes no contribution to the χ_1 or χ_2 score. For the detec-

tion of linkage, the scoring is based on the conditional probability for families having s children regardless of these phenotypes.

There is a four-fold classification of scores written in terms of χ_1 and χ_2:

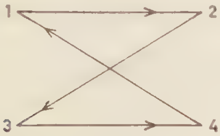
(1.) No children are rejected in scoring for χ_1 and χ_2.

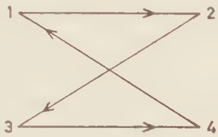
(2.) Some children are rejected in scoring for χ_1 but none are rejected in scoring for χ_2 (or vice versa).

(3.) The same children are rejected in scoring for χ_1 are χ_2.

(4.) Different children are rejected in scoring for χ_1 and χ_2.

Where A and B obey the dominance relations:





The phenotypes:

A_1B_1	A_4B_1	$A_1B_1B_3$	$A_4B_1B_3$
A_2B_1	A_3B_1	$A_2B_1B_3$	$A_3B_1B_3$
		A_1B_2	A_4B_2
		A_2B_2	A_3B_2

have for their probabilities:

$\frac{1-\chi_2}{4}$	$\frac{\chi_2}{4}$	$\frac{(1-\chi_1)\,\chi_2}{4}$	$\frac{(1-\chi_1)\,(1-\chi_2)}{4}$
$\frac{1-\chi_2}{4}$	$\frac{\chi_2}{4}$	$\frac{\chi_1\,\chi_2}{4}$	$\frac{\chi_1\,(1-\chi_2)}{4}$
		$\frac{\chi_1\,\chi_2}{4}$	$\frac{(\chi_1)\,(1-\chi_2)}{4}$
		$\frac{(1-\chi_1)\,\chi_2}{4}$	$\frac{(1-\chi_1)\,(1-\chi_2)}{4}$

In preparing the basic quantities for the λ_2 scores, all phenotypes contribute information on linkage and so none are rejected. The generating function is therefore based on the twelve phenotypes:

$$\Phi_2 = (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12)^s - (1, 2, 3, 4, 5, 6, 9, 10)^s.$$

In preparing the basic quantities for the λ_1 scores, the probabilities of the first four phenotypes: A_1B_1, A_2B_1, A_4B_1 and A_3B_1 are independent of χ_1 and each of their derivatives, f_i', is zero. Thus for scoring λ_1, all B_1 children are rejected. The conditional probabilities for scoring χ_1 are:

$$\frac{(1-\chi_1)\,\chi_2}{2} \qquad \frac{(1-\chi_1)\,(1-\chi_2)}{2}$$

$$\frac{\chi_1\,\chi_2}{2} \qquad \frac{\chi_1\,(1-\chi_2)}{2}$$

$$\frac{\chi_1\,\chi_2}{2} \qquad \frac{\chi_1\,(1-\chi_2)}{2}$$

$$\frac{(1-\chi_1)\,\chi_2}{2} \qquad \frac{(1-\chi_1)\,(1-\chi_2)}{2}$$

The generating function is based on the remaining eight phenotypes:

$$\Phi_1 = (1, 2, 3, 4, 5, 6, 7, 8)^s - (1, 2, 5, 6)^s.$$

Thus the λ_1 and λ_2 scores are each based upon different scorable family sizes because of the rejection of B_1 children.

The mating:

$$A_1A_2B_1B_2 \times A_3A_4B_1B_2$$

where neither factor shows dominance, illustrates the rejection of the same children when scoring for χ_1 and χ_2.

The phenotypes:

$A_1A_3B_1$	$A_1A_4B_1$		
$A_2A_3B_1$	$A_2A_4B_1$		
$A_1A_3B_1B_2$	$A_1A_4B_1B_2$	$A_1A_3B_2$	$A_1A_4B_2$
$A_2A_3B_1B_2$	$A_2A_4B_1B_2$	$A_2A_3B_2$	$A_2A_4B_2$

have for their probabilities:

$\frac{(1-\chi_1)\,(1-\chi_2)}{4}$	$\frac{(1-\chi_1)\,\chi_2}{4}$		
$\frac{\chi_1(1-\chi_2)}{4}$	$\frac{\chi_1\chi_2}{4}$		
$\frac{\chi_1+\chi_2-2\chi_1\chi_2}{4}$	$\frac{1-\chi_1-\chi_2+2\chi_1\chi_2}{4}$	$\frac{\chi_1\chi_2}{4}$	$\frac{\chi_1(1-\chi_2)}{4}$
$\frac{1-\chi_1-\chi_2+2\chi_1\chi_2}{4}$	$\frac{\chi_1+\chi_2-2\chi_1\chi_2}{4}$	$\frac{(1-\chi_1)\,\chi_2}{4}$	$\frac{(1-\chi_1)\,(1-\chi_2)}{4}$

In preparing the basic quantities for the scoring of this mating, the derivatives, f_1', f_2', of the probabilities of the four phenotypes:

$$A_1A_3B_1B_2$$
$$A_2A_3B_1B_2$$
$$A_1A_4B_1B_2$$
$$A_2A_4B_1B_2$$

are each zero and the four phenotypes contribute nothing to the scoring of χ_1 or χ_2. Hence B_1B_2 children are rejected. The conditional probabilities for scoring χ_1 and χ_2 are:

$$\frac{(1-\chi_1)(1-\chi_2)}{2} \qquad \frac{(1-\chi_1)\chi_2}{2}$$

$$\frac{\chi_1(1-\chi_2)}{2} \qquad \frac{\chi_1\chi_2}{2}$$

$$\frac{\chi_1\chi_2}{2} \qquad \frac{\chi_1(1-\chi_2)}{2}$$

$$\frac{(1-\chi_1)\chi_2}{2} \qquad \frac{(1-\chi_1)(1-\chi_2)}{2}$$

and all formulae for this mating will be based on this reduced family size.

Finally the mating:

$$A_1A_2B_1B_2 \times A_1A_3B_1B_2$$

used previously to illustrate *Bailey's* simplified approach may be referred to as an example of the rejection of different children in scoring for χ_1 and χ_2. Out of nine phenotypes from the mating, three were rejected in scoring for χ_1 and five were rejected in scoring for χ_2.

Even though such children are rejected in scoring systems for the detection of linkage, nevertheless the frequency of such children might be used in any efficient estimate of the recombination fraction provided the frequency is not independent of the recombination fraction.

The detection of linkage for two factors, neither showing dominance

The development of scores and the evaluation of the information contained in them are discussed only for mating types where one or both of the loci of two factors have a series of multiple allelomorphic genes and neither factor shows dominance.

To obtain information on linkage between two factors: A and B, it is necessary that at least one parent be heterozygous for both factors. Thus different mating types may be classified by the number of new or same

genes introduced into the mating by the parent homozygous for either or both factors. If both parents are heterozygous for both factors then it is immaterial which parent is used to introduce the new genes.

The numbers in the table below refer to the new genes which are introduced for the factors A and B respectively. They are assumed to be heterozygous in their locus unless an ho follows the number, in which case the gene is homozygous. (The symbol, ho, stands for homozygous.)

When at most four allelomorphic genes are involved, a five-fold classification of matings is possible for each factor. These are indicated as follows:

"2". If both parents are heterozygous in a factor and all four different allelomorphic genes contribute to the double heterozygosity, then the number, 2, designates this type of mating; e.g. $A_1A_3 \times A_2A_4$.

"1". If both parents are heterozygous in a factor and three different allelomorphic genes contribute to the double heterozygosity then the number, 1, designates this type of mating; e.g. $A_1A_2 \times A_2A_4$.

"0". If both parents are heterozygous in a factor and two different allelomorphic genes contribute to the double heterozygosity then the number, 0, designates this type of mating; e.g. $A_1A_2 \times A_1A_2$.

"1 ho". As indicated above, only one parent may be homozygous in either or both factors. If, in this parent, the homozygous gene does not exist in the homologous chromosomes of the heterozygous parent then the number, 1 ho, designates this type of mating; e.g. $A_1A_2 \times A_3A_3$.

"0 ho". If the homozygous gene exists in the homologous chromosomes of the heterozygous parent, the number 0 ho, designates this type of mating; e.g. $A_1A_2 \times A_2A_2$.

Applied independently to both test factors, A and B, the 5×5 or 25 mating types possible are listed in table 4. The first number refers to the A factor, the second to the B factor.

Table 4

Table of mating types

2 2	1 2	0 2	1 ho 2	0 ho 2
2 1	1 1	0 1	1 ho 1	0 ho 1
2 0	1 0	0 0	1 ho 0	0 ho 0
2 1 ho	1 1 ho	0 1 ho	1 ho 1 ho	0 ho 1 ho
2 0 ho	1 0 ho	0 0 ho	1 ho 0 ho	0 ho 0 ho

Since neither factor shows dominance, the same genotypic mating type is obtained when the numbers referring to A and B are interchanged, e.g. (1, 0 ho) and (0 ho, 1). Symmetry thus reduces the 25 mating types to 15. This enables us to standardize the entry of genes on factor A in the 15 mating types listed in table 5. Listed also is the number of phenotypes arising from the mating. An arrow indicates that in the evaluation of the score, the second number of phenotypes is used. *Finney's* three types for non-dominance are indicated in brackets.

Table 5

Reduced mating types

Factor A	Factor B	Number of Phenotypes
2	2	16
2	1	16
1	1	16
2	0	12→8
1	0	12→8
0	0	9→4 (F 22)
2	1 ho	8
2	0 ho	8
1	1 ho	8
1	0 ho	8
0	1 ho	4 (F 21)
0	0 ho	4
1 ho	1 ho	4 (F 20)
1 ho	0 ho	4
0 ho	0 ho	4

The first mating type yielding 16 phenotypes, is given by (2,2). The mating:

$$A_1A_2B_1B_2 \times A_3A_4B_3B_4$$

illustrates this type. The probabilities of the sixteen phenotypes from such a mating are given below with the two recombination fractions χ_1 and χ_2.

Since the probabilities are non-symmetrical in χ_1 and χ_2 and cannot be expressed as linear functions of χ^2, $\chi(1-\chi)$ or $(1-\chi)^2$, the primed equations, (1)′ and (2)′, will be used.

	A_3B_3	A_4B_3	A_3B_4	A_4B_4
A_1B_1	$\frac{(1-\chi_1)(1-\chi_2)}{4}$	$\frac{(1-\chi_1)\chi_2}{4}$	$\frac{(1-\chi_1)\chi_2}{4}$	$\frac{(1-\chi_1)(1-\chi_2)}{4}$
A_1B_2	$\frac{\chi_1(1-\chi_2)}{4}$	$\frac{\chi_1\chi_2}{4}$	$\frac{\chi_1\chi_2}{4}$	$\frac{\chi_1(1-\chi_2)}{4}$
A_2B_1	$\frac{\chi_1(1-\chi_2)}{4}$	$\frac{\chi_1\chi_2}{4}$	$\frac{\chi_1\chi_2}{4}$	$\frac{\chi_1(1-\chi_2)}{4}$
A_2B_2	$\frac{(1-\chi_1)(1-\chi_2)}{4}$	$\frac{(1-\chi_1)\chi_2}{4}$	$\frac{(1-\chi_1)\chi_2}{4}$	$\frac{(1-\chi_1)(1-\chi_2)}{4}$

To evaluate λ and I the following notation is useful. The observed frequencies are assumed to be written to conform with 16 phenotypes:

$$\begin{array}{cccc} a_1 & a_5 & a_9 & a_{13} \\ a_2 & a_6 & a_{10} & a_{14} \\ a_3 & a_7 & a_{11} & a_{15} \\ a_4 & a_8 & a_{12} & a_{16} \end{array}$$

When the notation

$$\begin{array}{|cccc|} \hline -2 & -2 & -2 & -2 \\ 2 & 2 & 2 & 2 \\ 2 & 2 & 2 & 2 \\ -2 & -2 & -2 & -2 \\ \hline \end{array}$$

is used

it is assumed that each of the numbers between the vincula is multiplied by its corresponding observed frequency, a_i, cell by cell and the products are added.

$$\bar{f} = \begin{array}{cccc} \hline {}^1/_{16} & {}^1/_{16} & {}^1/_{16} & {}^1/_{16} \\ {}^1/_{16} & {}^1/_{16} & {}^1/_{16} & {}^1/_{16} \\ {}^1/_{16} & {}^1/_{16} & {}^1/_{16} & {}^1/_{16} \\ {}^1/_{16} & {}^1/_{16} & {}^1/_{16} & {}^1/_{16} \\ \hline \end{array}$$

$$\bar{f}_1' = \begin{array}{cccc} \hline -{}^1/_8 & -{}^1/_8 & -{}^1/_8 & -{}^1/_8 \\ {}^1/_8 & {}^1/_8 & {}^1/_8 & {}^1/_8 \\ {}^1/_8 & {}^1/_8 & {}^1/_8 & {}^1/_8 \\ -{}^1/_8 & -{}^1/_8 & -{}^1/_8 & -{}^1/_8 \\ \hline \end{array} \qquad \bar{f}_2' = \begin{array}{cccc} \hline -{}^1/_8 & {}^1/_8 & {}^1/_8 & -{}^1/_8 \\ -{}^1/_8 & {}^1/_8 & {}^1/_8 & -{}^1/_8 \\ -{}^1/_8 & {}^1/_8 & {}^1/_8 & -{}^1/_8 \\ -{}^1/_8 & {}^1/_8 & {}^1/_8 & -{}^1/_8 \\ \hline \end{array}$$

$$\frac{\bar{f}'_1}{\bar{\bar{f}}} = \overline{\begin{matrix} -2 & -2 & -2 & -2 \\ 2 & 2 & 2 & 2 \\ 2 & 2 & 2 & 2 \\ -2 & -2 & -2 & -2 \end{matrix}} \qquad \frac{\bar{f}'_2}{\bar{\bar{f}}_2} = \overline{\begin{matrix} -2 & 2 & 2 & -2 \\ -2 & 2 & 2 & -2 \\ -2 & 2 & 2 & -2 \\ -2 & 2 & 2 & -2 \end{matrix}}$$

$$\frac{\bar{f}'^2_1}{\bar{\bar{f}}} = \frac{\bar{f}'^2_2}{\bar{\bar{f}}} = \overline{\begin{matrix} 1/4 & 1/4 & 1/4 & 1/4 \\ 1/4 & 1/4 & 1/4 & 1/4 \\ 1/4 & 1/4 & 1/4 & 1/4 \\ 1/4 & 1/4 & 1/4 & 1/4 \end{matrix}}$$

The appropriate score is obtained from substitution in (1)′

$$\lambda_1 = {}^1/_8 \left\{ \overline{\begin{matrix} -2 & -2 & -2 & -2 \\ 2 & 2 & 2 & 2 \\ 2 & 2 & 2 & 2 \\ -2 & -2 & -2 & -2 \end{matrix}}^2 - \overline{\begin{matrix} 4 & 4 & 4 & 4 \\ 4 & 4 & 4 & 4 \\ 4 & 4 & 4 & 4 \\ 4 & 4 & 4 & 4 \end{matrix}} \right\}$$

$$\lambda_2 = {}^1/_8 \left\{ \overline{\begin{matrix} -2 & 2 & 2 & -2 \\ -2 & 2 & 2 & -2 \\ -2 & 2 & 2 & -2 \\ -2 & 2 & 2 & -2 \end{matrix}}^2 - \overline{\begin{matrix} 4 & 4 & 4 & 4 \\ 4 & 4 & 4 & 4 \\ 4 & 4 & 4 & 4 \\ 4 & 4 & 4 & 4 \end{matrix}} \right\}$$

and from (2)′,

$$I_1 = 2.{}^1/_8{}^2\, s(s-1)\,(4^2) = {}^1/_2 s(s-1) = \omega_1 = I_2$$

$$\lambda_1 = {}^1/_2 \left\{ \overline{\begin{matrix} 1 & 1 & 1 & 1 \\ -1 & -1 & -1 & -1 \\ -1 & -1 & -1 & -1 \\ 1 & 1 & 1 & 1 \end{matrix}}^2 - \overline{\begin{matrix} 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 \end{matrix}} \right\}$$

$$\lambda_2 = {}^1/_2 \left\{ \overline{\begin{matrix} 1 & -1 & -1 & 1 \\ 1 & -1 & -1 & 1 \\ 1 & -1 & -1 & 1 \\ 1 & -1 & -1 & 1 \end{matrix}}^2 - \overline{\begin{matrix} 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 \end{matrix}} \right\}$$

The first part of the score is a function of χ_1, the second part a function of χ_2. In the χ_1 part of the score, the four observed frequencies in any one row may be grouped together under row headings: A_1B_1, A_2B_1, A_1B_2 and A_2B_2. These headings correspond to the a, b, c, d headings respectively in

Finney's table 1 (1940); a portion of which is reproduced in table 1. Similarly when scoring for χ_2, the column headings A_3B_3, A_4B_3, A_3B_4, and A_4B_4 correspond to the a, b, c and d headings of the same table. The score, λ, then consists of two parts each $^1/_2u_{11}$:

$$\lambda_1 = {}^1/_2\, u_{11}$$
$$\lambda_2 = {}^1/_2\, u_{11}$$

Where $u_{11} = (a-b-c+d)^2-(a+b+c+d)$.

The matings indicated by the classifications: (2, 2), (2, 1) and (1, 1) in table 5 are all scores in a similar manner and have the same amounts of information.

Matings yielding twelve phenotypes of which 8 are used in the scoring and information formulae follow from (2, 0) and (1, 0) in table 5. A mating in this classification is:

$$A_1A_2B_1B_2 \times A_3A_4B_1B_2.$$

The probabilities are:

	A_3B_1	A_4B_1	A_3B_2	A_4B_2
A_1B_1	$\frac{(1-\chi_1)(1-\chi_2)}{4}$	$\frac{(1-\chi_1)\chi_2}{4}$	$\frac{(1-\chi_1)\chi_2}{4}$	$\frac{(1-\chi_1)(1-\chi_2)}{4}$
A_2B_1	$\frac{\chi_1(1-\chi_2)}{4}$	$\frac{\chi_1\chi_2}{4}$	$\frac{\chi_1\chi_2}{4}$	$\frac{\chi_1(1-\chi_2)}{4}$
A_1B_2	$\frac{\chi_1(1-\chi_2)}{4}$	$\frac{\chi_1\chi_2}{4}$	$\frac{\chi_1\chi_2}{4}$	$\frac{\chi_1(1-\chi_2)}{4}$
A_2B_2	$\frac{(1-\chi_1)(1-\chi_2)}{4}$	$\frac{(1-\chi_1)\chi_2}{4}$	$\frac{(1-\chi_1)\chi_2}{4}$	$\frac{(1-\chi_1)(1-\chi_2)}{4}$

The phenotypes $A_1A_3B_1B_2$, $A_2A_3B_1B_2$, $A_1A_4B_1B_2$ and $A_2A_4B_1B_2$ occur in two parts of the diagram above. In evaluating the score for such a mating two methods may be adopted as *Finney* points out on p 13 of (1941, a) in the mating of MN × MN. The family may be considered as a member of a population of families having a given total number of children or as a member of a population of families having a reduced number of children (in the above case a given number of not B_1B_2 children). Since the B_1B_2 children contribute no information to the detection of linkage the latter course is adopted here. Eight phenotypes remain and their probabilities become:

	A_3B_1	A_4B_1	A_3B_2	A_4B_2
A_1B_1	$\dfrac{(1-\chi_1)(1-\chi_2)}{2}$	$\dfrac{(1-\chi_1)\chi_2}{2}$		
A_2B_1	$\dfrac{\chi_1(1-\chi_2)}{2}$	$\dfrac{\chi_1\chi_2}{2}$		
A_1B_2			$\dfrac{\chi_1\chi_2}{2}$	$\dfrac{\chi_1(1-\chi_2)}{2}$
A_2B_2			$\dfrac{(1-\chi_1)\chi_2}{2}$	$\dfrac{(1-\chi_1)(1-\chi_2)}{2}$

Since the probabilities are non-symmetrical in χ_1 and χ_2, the score will consist of two parts: one a function of χ_1, the other a function of χ_2. The equations (1)′ and (2)′ will be used. The appropriate constants are:

$$\overline{f} = \begin{bmatrix} 1/8 & 1/8 & \cdot & \cdot \\ 1/8 & 1/8 & \cdot & \cdot \\ \cdot & \cdot & 1/8 & 1/8 \\ \cdot & \cdot & 1/8 & 1/8 \end{bmatrix}$$

$$\overline{f}_1' = \begin{bmatrix} -1/4 & -1/4 & \cdot & \cdot \\ 1/4 & 1/4 & \cdot & \cdot \\ \cdot & \cdot & 1/4 & 1/4 \\ \cdot & \cdot & -1/4 & -1/4 \end{bmatrix} \qquad \overline{f}_2' = \begin{bmatrix} -1/4 & 1/4 & \cdot & \cdot \\ -1/4 & 1/4 & \cdot & \cdot \\ \cdot & \cdot & 1/4 & -1/4 \\ \cdot & \cdot & 1/4 & -1/4 \end{bmatrix}$$

$$\frac{\overline{f}_1'}{\overline{f}} = \begin{bmatrix} -2 & -2 & \cdot & \cdot \\ 2 & 2 & \cdot & \cdot \\ \cdot & \cdot & 2 & 2 \\ \cdot & \cdot & -2 & -2 \end{bmatrix} \qquad \frac{\overline{f}_2'}{\overline{f}} = \begin{bmatrix} -2 & 2 & \cdot & \cdot \\ -2 & 2 & \cdot & \cdot \\ \cdot & \cdot & 2 & -2 \\ \cdot & \cdot & 2 & -2 \end{bmatrix}$$

$$\frac{\overline{f}_1'^2}{\overline{f}} = \frac{\overline{f}_2'^2}{\overline{f}} = \begin{bmatrix} 1/2 & 1/2 & \cdot & \cdot \\ 1/2 & 1/2 & \cdot & \cdot \\ \cdot & \cdot & 1/2 & 1/2 \\ \cdot & \cdot & 1/2 & 1/2 \end{bmatrix}$$

Hence after some reduction,

$$\lambda_1 = 1/2 \left\{ \begin{bmatrix} 1 & 1 & \cdot & \cdot \\ -1 & -1 & \cdot & \cdot \\ \cdot & \cdot & -1 & -1 \\ \cdot & \cdot & 1 & 1 \end{bmatrix}^2 - \begin{bmatrix} 1 & 1 & \cdot & \cdot \\ 1 & 1 & \cdot & \cdot \\ \cdot & \cdot & 1 & 1 \\ \cdot & \cdot & 1 & 1 \end{bmatrix} \right\}$$

$$\lambda_2 = {}^1/_2 \left\{ \overline{\underline{\begin{array}{cccc} 1 & -1 & . & . \\ 1 & -1 & . & . \\ . & . & -1 & 1 \\ . & . & -1 & 1 \end{array}}}^{\,2} - \overline{\underline{\begin{array}{cccc} 1 & 1 & . & . \\ 1 & 1 & . & . \\ . & . & 1 & 1 \\ . & . & 1 & 1 \end{array}}} \right\}$$

$$\lambda_1 = {}^1/_2\, u_{11}$$
$$\lambda_2 = {}^1/_2\, u_{11}$$

The amount of information is given by:

$$I_1 = 2.{}^1/_8{}^2\, s(s-1)\,(4^2) = {}^1/_2 s(s-1) = \omega_1 = I_2.$$

The matings under the classifications (2, 1 ho), (2, 0 ho), (1, 1 ho) and (1, 0 ho) from table 5 yield 8 phenotypes directly. Consider the mating:

$$A_1A_2B_1B_2 \times A_3A_4B_3B_3$$

The probabilities, f_i, are linear in χ_1 so equations (1) and (2) are used in evaluating λ_1 and I_1. The probabilities are given below.

	A_3B_3	A_4B_3
A_1B_1	$\frac{(1-\chi_1)}{4}$	$\frac{(1-\chi_1)}{4}$
A_2B_1	$\frac{\chi_1}{4}$	$\frac{\chi_1}{4}$
A_1B_2	$\frac{\chi_1}{4}$	$\frac{\chi_1}{4}$
A_2B_2	$\frac{(1-\chi_1)}{4}$	$\frac{(1-\chi_1)}{4}$

The constants needed for evaluation of λ_1 and I_1 are:

$$\bar{f} = \overline{\underline{\begin{array}{cc} {}^1/_8 & {}^1/_8 \\ {}^1/_8 & {}^1/_8 \\ {}^1/_8 & {}^1/_8 \\ {}^1/_8 & {}^1/_8 \end{array}}} \qquad \bar{f}_1' = \overline{\underline{\begin{array}{cc} -{}^1/_4 & -{}^1/_4 \\ {}^1/_4 & {}^1/_4 \\ {}^1/_4 & {}^1/_4 \\ -{}^1/_4 & -{}^1/_4 \end{array}}}$$

$$\frac{\bar{f}_1'}{\bar{f}} = \overline{\underline{\begin{array}{cc} -2 & -2 \\ 2 & 2 \\ 2 & 2 \\ -2 & -2 \end{array}}} \qquad \frac{\bar{f}_1'^2}{\bar{f}} = \overline{\underline{\begin{array}{cc} {}^1/_2 & {}^1/_2 \\ {}^1/_2 & {}^1/_2 \\ {}^1/_2 & {}^1/_2 \\ {}^1/_2 & {}^1/_2 \end{array}}}$$

$$\text{Hence } \lambda_1 = {}^1/_8 \left\{ \begin{vmatrix} -2 & -2 \\ 2 & 2 \\ 2 & 2 \\ -2 & -2 \end{vmatrix}^2 - \begin{vmatrix} 4 & 4 \\ 4 & 4 \\ 4 & 4 \\ 4 & 4 \end{vmatrix} \right\}$$

$$\lambda_1 = {}^1/_2\, u_{11}$$

and $I_1 = 2.{}^1/_8{}^2\, s(s-1)\,.\,4^2 = {}^1/_2 s(s-1) = \omega_1$.

The last three mating types in table 5 are *Finney*'s 22, 21 and 20. Matings of the type (0, 0) give *Finney*'s type 22. Consider the mating:

$$A_1A_2B_1B_2 \times A_1A_2B_1B_2$$

This yields nine possible genotypes which can be distinguished phenotypically. If a family is considered as a member of a family having a given number of not A_1A_2, not B_1B_2 children and χ_1 is assumed not necessarily equal to χ_2, the probabilities of the four remaining phenotypes become:

	A_1B_1	A_2B_1	A_1B_2	A_2B_2
A_1B_1	$(1-\chi_1)(1-\chi_2)$	—	—	—
A_2B_1	—	$\chi_1\chi_2$	—	—
A_1B_2	—	—	$\chi_1\chi_2$	—
A_2B_2	—	—	—	$(1-\chi_1)(1-\chi_2)$

The probabilities are not linear functions of either χ or θ but are symmetrical in χ_1 and χ_2. Hence we need to differentiate with respect to, say, χ_1 only. The constants for substitution in (3)′ and (4)′ are:

$$\bar{f} = \begin{vmatrix} {}^1/_4 & \cdot & \cdot & \cdot \\ \cdot & {}^1/_4 & \cdot & \cdot \\ \cdot & \cdot & {}^1/_4 & \cdot \\ \cdot & \cdot & \cdot & {}^1/_4 \end{vmatrix} \qquad \bar{f}_1' = \begin{vmatrix} {}^1/_2 & \cdot & \cdot & \cdot \\ \cdot & {}^1/_2 & \cdot & \cdot \\ \cdot & \cdot & {}^1/_2 & \cdot \\ \cdot & \cdot & \cdot & -{}^1/_2 \end{vmatrix}$$

$$\frac{\bar{f}_1'}{\bar{f}} = \begin{vmatrix} -2 & \cdot & \cdot & \cdot \\ \cdot & 2 & \cdot & \cdot \\ \cdot & \cdot & 2 & \cdot \\ \cdot & \cdot & \cdot & -2 \end{vmatrix} \qquad \frac{\bar{f}_1'^2}{\bar{f}} = \begin{vmatrix} 1 & \cdot & \cdot & \cdot \\ \cdot & 1 & \cdot & \cdot \\ \cdot & \cdot & 1 & \cdot \\ \cdot & \cdot & \cdot & 1 \end{vmatrix}$$

Since $c_i = {}^1/_4$ then

$$\lambda = {}^1/_4 \left\{ \overline{\begin{vmatrix} -2 & . & . & . \\ . & 2 & . & . \\ . & . & 2 & . \\ . & . & . & -2 \end{vmatrix}}^{\,2} - \overline{\begin{vmatrix} 4 & . & . & . \\ . & 4 & . & . \\ . & . & 4 & . \\ . & . & . & 4 \end{vmatrix}} \right\} = u_{11}$$

and $I = 2 \,.\, {}^1/_4{}^2\, s\,(s-1)\, 4^2 = 2s\,(s-1) = 4\,\omega_1$.

The above expressions for λ and I are based on the assumption that we are interested in the recombination fraction χ. If for some reason we are interested in the recombination fraction of, say, females, on the assumption that $\chi_1 = {}^1/_2$ then we proceed as follows. In this case the probabilities are given below:

	f
A_1B_1	$\frac{1-\chi_2}{2}$
A_2B_1	$\frac{\chi_2}{2}$
A_1B_2	$\frac{\chi_2}{2}$
A_2B_2	$\frac{1-\chi_2}{2}$

The constants for substitution in (1) and (2) are those given above but c_i is now ${}^1/_8$. Their substitution in (1) and (2) yield:

$$\lambda_{2\,.\,1} = {}^1/_2 u_{11}$$
$$I_{2\,.\,1} = 2 \,.\, {}^1/_8{}^2\, s\,(s-1) \,.\, 4^2 = \omega_1$$

It must be emphasized here that scores $\lambda_{2\,.\,1}$ and $\lambda_{1\,.\,2}$ cannot be formed simultaneously in the same problem since the same phenotypes are used in each.

Matings of the type (0, 0 ho) of table 5 yield 6 genotypes distinguishable phenotypically and are of *Finney's* type 21. Consider the mating:

$$A_1A_2B_1B_2 = A_1A_2B_3$$

The probabilities of the six phenotypes are:

	A_1B_3	A_2B_3
A_1B_1	$\frac{(1-\chi_1)}{4}$	$\frac{(1-\chi_1)}{4}$
A_2B_1	$\frac{\chi_1}{4}$	$\frac{\chi_1}{4}$
A_1B_2	$\frac{\chi_1}{4}$	$\frac{\chi_1}{4}$
A_2B_2	$\frac{(1-\chi_1)}{4}$	$\frac{(1-\chi_1)}{4}$

On rejecting the A_1A_2 children, the probabilities are linear in χ_1 and become:

	A_1B_3	A_2B_3
A_1B_1	$\frac{(1-\chi_1)}{2}$	–
A_2B_1	–	$\frac{\chi_1}{2}$
A_1B_2	$\frac{\chi_1}{2}$	–
A_2B_2	–	$\frac{(1-\chi_1)}{2}$

The constants for substitution in (1) and (2) are:

$$\overline{f} = \begin{array}{cc} {}^1/_4 & . \\ . & {}^1/_4 \\ {}^1/_4 & . \\ . & {}^1/_4 \end{array} \qquad \overline{f}_1' = \begin{array}{cc} -{}^1/_2 & . \\ . & {}^1/_2 \\ {}^1/_2 & . \\ . & -{}^1/_2 \end{array}$$

$$\frac{\overline{f}_1'}{\overline{f}} = \begin{array}{cc} -2 & . \\ . & 2 \\ 2 & . \\ . & -2 \end{array} \qquad \frac{\overline{f}_1'^2}{\overline{f}} = \begin{array}{cc} 1 & . \\ . & 1 \\ 1 & . \\ . & 1 \end{array}$$

Hence

$$\lambda_1 = {}^1/_8 \left\{ \begin{array}{cc} -2 & . \\ . & 2 \\ 2 & . \\ . & -2 \end{array}^{2} - \begin{array}{cc} 4 & . \\ . & 4 \\ 4 & . \\ . & 4 \end{array} \right\} = {}^1/_2 u_{11}$$

Table 6

Table of scores, neither factor showing dominance

Class	Mating type	Mating	Number of pheno-types	χ	a	b	c	d	λ	I	Reject children whose Phenotypes are	*Finney's* type
(2, 2)	1	$A_1A_2B_1B_2 \times A_3A_4B_3B_4$	16	χ_1	$A_1A_3B_1B_3$	$A_2A_3B_1B_3$	$A_1A_3B_2B_3$	$A_2A_3B_2B_3$	$^1/_2u_{11}$	ω_1		
					$A_1A_4B_1B_3$	$A_2A_4B_1B_3$	$A_1A_4B_2B_3$	$A_2A_4B_2B_3$				
					$A_1A_3B_1B_4$	$A_2A_3B_1B_4$	$A_1A_3B_2B_4$	$A_2A_3B_2B_4$				
					$A_1A_4B_1B_4$	$A_2A_4B_1B_4$	$A_1A_4B_2B_4$	$A_2A_4B_2B_4$				
				χ_2	$A_1A_3B_1B_3$	$A_1A_4B_1B_3$	$A_1A_3B_1B_4$	$A_1A_4B_1B_4$	$^1/_2u_{11}$	ω_1		
					$A_2A_3B_1B_3$	$A_2A_4B_1B_3$	$A_2A_3B_1B_4$	$A_2A_4B_1B_4$				
					$A_1A_3B_2B_3$	$A_1A_4B_2B_3$	$A_1A_3B_2B_4$	$A_1A_4B_2B_4$				
					$A_2A_3B_2B_3$	$A_2A_4B_2B_3$	$A_2A_3B_2B_4$	$A_2A_4B_2B_4$				
(2, 1)		$A_1A_2B_1B_2 \times A_3A_4B_1B_3$	16		replace B_4 in each phenotype above by B_1							
		$\times A_3A_4B_2B_3$	16		replace B_4 in each phenotype above by B_2							
(1, 1)		$A_1A_2B_1B_2 \times A_1A_3B_1B_3$	16		replace A_4, B_4, in each phenotype above by A_1, B_1 respectively							
		$\times A_2A_3B_1B_3$	16		replace A_4, B_4, in each phenotype above by A_2, B_1 respectively							
		$\times A_1A_3B_2B_3$	16		replace A_4, B_4, in each phenotype above by A_1, B_2 respectively							
		$\times A_2A_3B_2B_3$	16		replace A_4, B_4, in each phenotype above by A_2, B_2 respectively							
(2, 0)	2	$A_1A_2B_1B_2 \times A_3A_4B_1B_2$	$12 \to 8$	χ_1	$A_1A_3B_1B_1$	$A_2A_3B_1B_1$	$A_1A_3B_2B_2$	$A_2A_3B_2B_2$	$^1/_2u_{11}$	ω_1	B_1B_2	
					$A_1A_4B_1B_1$	$A_2A_4B_1B_1$	$A_1A_4B_2B_2$	$A_2A_4B_2B_2$				
				χ_2	$A_1A_3B_1B_1$	$A_1A_4B_1B_1$	$A_1A_3B_2B_2$	$A_1A_4B_2B_2$	$^1/_2u_{11}$	ω_1		
					$A_2A_3B_1B_1$	$A_2A_4B_1B_1$	$A_2A_3B_2B_2$	$A_2A_4B_2B_2$				
(1, 0)		$A_1A_2B_1B_2 \times A_1A_3B_1B_2$			replace A_4 in each phenotype above by A_1							
		$\times A_2A_3B_1B_2$			replace A_4 in each phenotype above by A_2							

(2, 1 ho)	3	$A_1A_2B_1B_2 \times A_3A_4B_3$	8	χ_1	$A_1A_3B_1B_3$ $A_2A_3B_1B_3$ $A_1A_3B_2B_3$ $A_2A_3B_2B_3$ $A_1A_4B_1B_3$ $A_2A_4B_1B_3$ $A_1A_4B_2B_3$ $A_2A_4B_2B_3$	$^1/_2u_{11}$	ω_1		
(2, 0 ho)		$A_1A_2B_1B_2 \times A_3A_4B_1$ $\times A_3A_4B_2$			replace B_3 in each phenotype above by B_1 replace B_3 in each phenotype above by B_2				
(1, 1 ho)		$A_1A_2B_1B_2 \times A_1A_3B_3$ $\times A_2A_3B_3$			replace A_4 in each phenotype above by A_1 replace A_4 in each phenotype above by A_2				
(1, 0 ho)		$A_1A_2B_1B_2 \times A_1A_3B_1$			replace A_4 and B_3 in each phenotype above by A_1 and B_1 respectively				
		$\times A_2A_3B_1$			replace A_4 and B_3 in each phenotype above by A_2 and B_1 respectively				
		$\times A_1A_3B_2$			replace A_4 and B_3 in each phenotype above by A_1 and B_2 respectively				
		$\times A_2A_3B_2$			replace A_4 and B_3 in each phenotype above by A_2 and B_2 respectively				
(0, 0)	4	$A_1A_2B_1B_2 \times A_1A_2B_1B_2$	$9 \to 4$	χ	A_1B_1 A_2B_1 A_1B_2 A_2B_2	u_{11}	$4\,\omega_1$	A_1A_2 and B_1B_2	22
(0, 1 ho)	5	$A_1A_2B_1B_2 \times A_1A_2B_3$	$6 \to 4$	χ_1	$A_1A_1B_1B_3$ $A_1A_1B_2B_3$ $A_2A_2B_1B_3$ $A_2A_2B_2B_3$	$^1/_2u_{11}$	ω_1	A_1A_2	21
(0, 0ho)		$A_1A_2B_1B_2 \times A_1A_2B_1$ $\times A_1A_2B_2$			replace B_3 in each phenotype above by B_1 replace B_3 in each phenotype above by B_2				
(1 ho, 0ho)	6	$A_1A_2B_1B_2 \times A_3B_3$	4	χ_1	$A_1A_3B_1B_3$ $A_2A_3B_1B_3$ $A_1A_3B_2B_3$ $A_2A_3B_2B_3$	$^1/_2u_{11}$	ω_1		20
(1, 0 ho)		$\times A_3B_2$ $\times A_3B_1$			replace B_3 in each phenotype above by B_2 replace B_3 in each phenotype above by B_1				
(0 ho, 0 ho)		$\times A_2B_1$			replace A_3 and B_3 in each phenotype above by A_2 and B_1 respectively				
		$\times A_1B_2$			replace A_3 and B_3 in each phenotype above by A_1 and B_2 respectively				

and $I_1 = 2 \cdot {}^1/_8{}^2\, s\,(s-1)\, 4^2 = {}^1/_2 s\,(s-1) = \omega_1$.

Finney's type 20 is obtained from matings classified as (1 ho, 1 ho), (1 ho, 0 ho) and (0 ho, 0 ho) of table 5. An example of this type is the mating:

$$A_1A_2B_1B_2 \times A_3B_3$$

The statistics required for substitution in (1) and (2) are:

	f	$\overline{f_1}$	$\overline{f_1'}$	$\frac{\overline{f_1'}}{\overline{f}}$	$\frac{\overline{f_1'^2}}{\overline{f}}$
A_1B_1	$\frac{(1-\chi_1)}{2}$	$^1/_4$	$-^1/_2$	-2	1
A_2B_1	$\frac{\chi_1}{2}$	$^1/_4$	$^1/_2$	2	1
A_1B_2	$\frac{\chi_1}{2}$	$^1/_4$	$^1/_2$	2	1
A_2B_2	$\frac{(1-\chi_1)}{2}$	$^1/_4$	$-^1/_2$	-2	$^1/_4$

Hence

$$\lambda_1 = {}^1/_8 \left\{ \begin{matrix} \overline{-2}^{\,2} \\ 2 \\ 2 \\ \underline{-2} \end{matrix} \quad - \quad \begin{matrix} \overline{4} \\ 4 \\ 4 \\ \underline{4} \end{matrix} \right\} = {}^1/_2 u_{11}$$

and $I_1 = 2 \cdot {}^1/_8{}^2\, s\,(s-1)\, 4^2 = {}^1/_2 s\,(s-1) = \omega_1$.

This completes the mating types for non-dominant factors.

Table 6 gives the scoring systems for the fifteen mating types when neither factor shows dominance. The remaining ten mating types, which are symmetrical to those discussed in the table, are scored by interchanging A and B in the body of the table. For example the mating:

$$A_1A_2B_1B_2 \times A_1A_2B_3B_4 \text{ which is a } (0,2)$$

will be scored as (2,0) upon interchanging A and B in the table. All A_1A_2 children will be rejected and the remaining phenotypes scored as below:

	a	b	c	d	λ	I
χ_1	A_1B_1	A_1B_2	A_2B_1	A_2B_2	$^1/_2 u_{11}$	ω_1
χ_2	A_1B_3	A_1B_4	A_2B_3	A_2B_4	$^1/_2 u_{11}$	ω_1

In the third column is listed the number of possible phenotypes arising from the mating in the second column. An arrow to a lower number indicates that certain phenotypes are rejected in scoring and the smaller number of phenotypes is used when evaluating the score.

The steps used in testing linkage between two factors, neither of which shows dominance, for table 6 follow closely those of *Finney* (1940) and are given below:

(1.) Classify the families according to parental phenotype. Families in which neither parent is doubly heterozygous are rejected.

(2.) Entry into table 9 is facilitated by examination of the number of genes involved in each factor. Column 1 lists these.

(3.) Determine the phenotypes of the children of the mating. The children of each family are then distributed among the four classes: a, b, c, d, according to the scheme in column 5. The last column shows the phenotypes of children rejected in forming the score.

(4.) Construct the score according to the functions in column 6. In the case of matings involving non-dominant factors, there are no score correction factors to be considered. Whenever the score consists of two u-statistics, the arrangements of the phenotypes for χ_1 differs from that of χ_2 and both segregations contribute to the total score as shown in column 6.

(5.) Amounts of information provided by the score in the absence of linkage are given in column 7. Where there are two segregations as in types 1, 2 and 3 each makes its individual contribution to the total amount of information.

(6.) Sum the scores for linkage and the amounts of information for the different matings and obtain $\Sigma\lambda$ and ΣI. The total information is also the variance of the score. The test of significance for linkage is the χ^2 with one degree of freedom:

$$\chi^2 = \frac{(\Sigma\ \lambda)^2}{\Sigma\ \mathrm{I}}$$

(7.) If the null hypothesis is rejected then an estimate of the recombination fraction, under procedure 1 is:

$$\tfrac{1}{2}\left\{1 - \left(\frac{\Sigma\ \lambda}{\Sigma\ \mathrm{I}}\right)^{1/2}\right\}$$

In the sections which follow, use is made of the symbolism of three fundamentals of propositions, (*Whitehead and Russell*, 1910): the contradictory function, the logical sum and the logical product. The symbol, $\sim A_1$, as used in the tables of scoring systems means that phenotype A_1 does

not exist, that is to say, that in the children of a specific mating no phenotypes A_1 are found. The symbol, $A_1 \vee A_2$ means that at least there exists A_1 or A_2, not excluding the case in which both exist. The symbol, $A_1 \,.\, A_2$, means that there exists both A_1 and A_2 phenotypes. When brackets are used, they have the ordinary algebraic meanings.

The expression:

$$[A_2A_4 \vee (A_2 \,.\, A_4)] \,.\, [B_2B_4 \vee B_2 \,.\, B_4]$$

means there exists a phenotype A_2A_4 and, or (A_2 and A_4) for the A factor together with a phenotype B_2B_4 and, or (B_2 and B_4) for the B factor. Similarly the expression:

$$[A_2 \sim A_4 \sim A_2A_4] \,.\, [\sim B_2 \sim B_4 \sim B_2B_4]$$

means there exists an A_2 child but no A_4 nor A_2A_4 children for the A factor together with no B_2 nor B_4 nor B_2B_4 children for the B factor.

One factor ABO blood group system, other factor non-dominant

Consider now matings arising when one factor, A, is the ABO blood group system and the second factor, B, consisting of two allelomorphic genes, shows no dominance.

The genotypes for each factor in this system are:

A_1A_1			B_1B_1
A_1A_2	A_2A_2		B_1B_2
A_1A_3	A_2A_3	A_3A_3	B_2B_2

The phenotypes are for each factor:

A_1	B_1
A_2	B_1B_2
A_3	B_2
A_1A_2	

These are therefore $4 \times 3 = 12$ phenotypes possible in the matings in this genetic system. In the mating diagram there are 144 possible matings which may be arranged as 16 squares of 9 matings each.

The scorable matings are classified below in three broad categories as they would occur in the mating diagram.

I Diagonal matings in diagonal squares:

1. $A_1A_2B_2 \times A_1B_1B_2$
2. $A_1A_2B_1B_2 \times A_1A_2B_1B_2$

II Diagonal matings in non-diagonal squares:

3. $A_1B_1B_2 \times A_2B_1B_2$
4. $A_1B_1B_2 \times A_3B_1B_2$
5. $A_1A_2B_1B_2 \times A_1B_1B_2$

Non-diagonal matings in diagonal squares:

6. $A_1B_1B_2 \times A_1B_1$
7. $A_1A_2B_1B_2 \times A_1A_2B_1$

III Non-diagonal matings in non-diagonal squares:

8. $A_1B_1B_2 \times A_1A_2B_1$
9. $A_1A_2B_1B_2 \times A_1B_1$
10. $A_1B_1B_2 \times A_2B_1$
11. $A_1B_1B_2 \times A_3B_1$

The phenotypes of the children of each of the above matings are now used in a logical approach to determine if both parents are doubly heterozygous in both factors, heterozygous in both factors for one parent only or not proven heterozygous for either parent in both factors.

Consider the mating:

$$A_1 \times A_2.$$

The genotypes possible in this mating are:

$$\begin{array}{ccc} A_1A_1 & \times & A_2A_2 \\ A_1A_3 & & A_2A_3 \end{array}$$

If these possible parental phenotypes be arranged as in table 3, then the various phenotypes of children necessary for the certainty of matings may be found.

Childrens' phenotypes

		A_1	A_2	A_3	A_1A_2
	$A_1A_1 \times A_2A_2$				$\times$
Parental	$A_1A_1 \times A_2A_3$	$\times$			$\times$
Phenotypes	$A_1A_3 \times A_2A_2$		$\times$		$\times$
	$A_1A_3 \times A_2A_3$	$\times$	$\times$	$\times$	$\times$

Thus if $A_3 \vee A_1 \cdot A_2$, (if $\exists$ A_3 and, or (A_1 and A_2)) children the mating is certain for both parents in this factor, if $A_1 \sim A_3 \sim A_2$, the mating is certain for second parent, if $A_2 \sim A_3 \sim A_1$, then the mating is certain for first parent, if $\sim A_1 \sim A_2 \sim A_3$, the mating is uncertain for both parents.

The logical approach is given below diagramatically for the mating:

$$A_1 \times A_2$$

$\exists A_3$? <
- yes, $A_1A_3 \times A_2A_3$
- no, $\exists A_2$? <
  - yes, $A_1 \times A_2A_3$ — $\exists A_2$? <
    - yes, $A_1A_3 \times A_2A_3$
    - no, $A_1 \times A_2A_3$
  - no, $\exists A_2$? <
    - yes, $A_1A_3 \times A_2$
    - no, $A_1 \times A_2$

The expression, $\exists A_3$? means "Does there exist an A_3 child?".

The two scorable matings from the mating type:

$$A_1B_1B_2 \times A_2B_1B_2$$

are: (i) if $A_3 \vee (A_1 \cdot A_2)$, $A_1A_3B_1B_2 \times A_2A_3B_1B_2$,

(ii) if $A_2 \sim A_3 \sim A_1$, $A_1A_3B_1B_2 \times A_2B_1B_2$,

or by symmetry, if $A_1 \sim A_3 \sim A_2$, $A_1A_1B_2 \times A_2A_3B_1B_2$.

The remaining mating, $A_1B_1B_2 \times A_2B_1B_2$, is not proven to be heterozygous for either parent in both factors and so will not be scored by these methods.

Recorded in table 7 are the eleven mating types listed by phenotypes together with the phenotypes of the children necessary to establish heterozygous matings for one or both parents.

Whenever the first parent is scored separately from the second parent as in mating types 3 and 5 of table 7, each part is allowed to make its own contribution to the total score and variance. No new formulae for the amounts of information are needed for this table as *Finney*, 1940, gives all the necessary values for I for families up to $s = 16$.

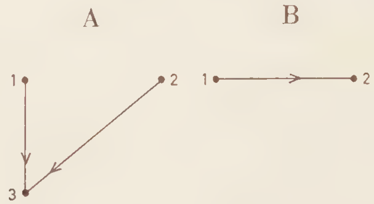
Table 7

Table of scores, one factor ABO blood group, other factor non-dominant

Type	Mating by phenotypes	If there exist children for Factor A	Mating is proven to be	χ	a	b	c	d	λ	I	Reject children	*Finney's* type
1	$A_1B_1B_2 \times A_1B_1B_2$	A_3	$A_1A_3B_1B_2 \times A_1A_3B_1B_2$	χ	A_1B_2	A_3B_2	A_1B_1	A_3B_1	$^1/_9u_{31}$	$4\,\omega_2$	(B_1B_2)	19
2	$A_1A_2B_1B_2 \times A_1A_2B_1B_2$		$A_1A_2B_1B_2 \times A_1A_2B_1B_2$	χ	A_1B_1	A_2B_1	A_1B_2	A_2B_2	u_{11}	$4\,\omega_1$	$(A_1A_2)\cdot(B_1B_2)$	22
3	$A_1B_1B_2 \times A_2B_1B_2$	A_3 $(A_1\cdot A_2)$	$A_1A_3B_1B_2 \times A_2A_3B_1B_2$	χ_1	$A_1A_2B_1$	A_2B_1	$A_1A_2B_2$	A_2B_2	$^1/_2u_{11}$	ω_1	(B_1B_2)	
					A_1B_1	A_3B_1	A_1B_2	A_3B_2	$^1/_2u_{11}$	ω_1		
				χ_2	$A_1A_2B_1$	A_1B_1	$A_1A_2B_2$	A_1B_2	$^1/_2u_{11}$	ω_1	(B_1B_2)	
					A_2B_1	A_3B_1	A_2B_2	A_3B_2	$^1/_2u_{11}$	ω_1		
		$A_2 \sim A_3 \sim A_1$	$A_1A_3B_1B_2 \times A_2B_1B_2$	χ_1	$A_1A_2B_1$	A_2B_1	$A_1A_2B_2$	A_2B_2	$^1/_2u_{11}$	ω_1	(B_1B_2)	
4	$A_1B_1B_2 \times A_3B_1B_2$	A_3	$A_1A_3B_1B_2 \times A_3B_1B_2$	χ_1	A_1B_1	A_3B_1	A_1B_2	A_3B_2	$^1/_2u_{11}$	ω_1	(B_1B_2)	17
5	$A_1A_2B_1B_2 \times A_1B_1B_2$	A_2	$A_1A_2B_1B_2 \times A_1A_3B_1B_2$	χ_1	A_1B_1	$A_1A_2B_1$	A_1B_2	$A_1A_2B_2$	$^1/_2u_{11}$	ω_1	(B_1B_2)	21′
						A_2B_1		A_2B_2				
				χ_2	$A_1A_2B_1$	A_2B_1	$A_1A_2B_2$	A_2B_2	$^1/_2u_{11}$	ω_1	$(A_1)\cdot(B_1B_2)$	21′
		$\sim A_2$	$A_1A_2B_1B_2 \times A_1B_1B_2$	χ_1	A_1B_1	$A_1A_2B_1$	A_1B_2	$A_1A_2B_2$	$^1/_2u_{11}$	ω_1	(B_1B_2)	21′
6	$A_1B_1B_2 \times A_1B_1$	A_3	$A_1A_3B_1B_2 \times A_1A_3B_1$	χ_1	A_1B_1	A_3B_1	$A_1B_1B_2$	$A_3B_1B_2$	$^1/_{18}u_{31}$	ω_2		18
7	$A_1A_2B_1B_2 \times A_1A_2B_1$		$A_1A_2B_1B_2 \times A_1A_2B_1$	χ_1	A_1B_1	A_2B_1	$A_1B_1B_2$	$A_2B_1B_2$	$^1/_2u_{11}$	ω_1	(A_1A_2)	21
8	$\times A_1A_2B_1$	A_2	$A_1A_3B_1B_2 \times A_1A_2B_1$	χ_1	$A_1A_2B_1$	A_2B_1	$A_1A_2B_1B_2$	$A_2B_1B_2$	$^1/_2u_{11}$	ω_1	(A_1)	16′
9	$A_1A_2B_1B_2 \times A_1B_1$	A_2	$A_1A_2B_1B_2 \times A_1A_3B_1$	χ_1	A_1B_1	$A_1A_2B_1$	$A_1B_1B_2$	$A_1A_2B_1B_2$	$^1/_2u_{11}$	ω_1		20′
						A_2B_1		$A_2B_1B_2$				
10	$A_1B_1B_2 \times A_2B_1$	A_3 $(A_1\cdot A_2)$	$A_1A_3B_1B_2 \times A_2A_3B_1$	χ_1	$A_1A_2B_1$	A_2B_1	$A_1A_2B_1B_2$	$A_2B_1B_2$	$^1/_2u_{11}$	ω_1		
					A_1B_1	A_3B_1	$A_1B_1B_2$	$A_3B_1B_2$				
		$A_2 \sim A_3 \sim A_1$	$A_1A_3B_1B_2 \times A_2B_1$	χ_1	$A_1A_2B_1$	A_2B_1	$A_1A_2B_1B_2$	$A_2B_1B_2$	$^1/_2u_{11}$	ω_1		
11	$A_1B_1B_2 \times A_3B_1$	A_3	$A_1A_3B_1B_2 \times A_3B_1$	χ_1	A_1B_1	A_3B_1	$A_1B_1B_2$	$A_3B_1B_2$	$^1/_2u_{11}$	ω_1		16

One factor ABO blood group system, other factor dominant

If the A factor is the ABO blood group system and the B factor consists of two allelomorphic genes with B_1 dominant to B_2, then the genetic system is:



The genotypes for each factor in this system are:

A_1A_1			B_1B_1
A_1A_2	A_2A_2		B_1B_2
A_1A_3	A_2A_3	A_3A_3	B_2B_2

The phenotypes for each factor are:

A_1	B_1
A_2	B_2
A_3	
A_1A_2	

Thus there are $2 \times 4 = 8$ possible phenotypes:

A_1B_1	A_2B_1	A_3B_1	$A_1A_2B_1$
A_1B_2	A_2B_2	A_3B_2	$A_1A_2B_2$

in the matings in this genetic system. In the mating diagram there are $8^2 = 64$ possible matings which may be arranged as 16 squares of 4 matings each.

The scorable matings are classified below in these broad categories as they would occur in the mating diagram.

I Diagonal matings in diagonal squares:

1. $A_1B_1 \times A_1B_1$
2. $A_1A_2B_1 \times A_1A_2B_1$

II Diagonal matings in non-diagonal squares:

3. $A_1B_1 \times A_2B_1$
4. $A_1B_1 \times A_3B_1$
5. $A_1A_2B_1 \times A_1B_1$

Non-diagonal matings in non-diagonal squares:
6. $A_1B_1 \times A_1B_2$
7. $A_1A_2B_1 \times A_1A_2B_2$

III Non-diagonal matings in non-diagonal squares:
8. $A_1B_1 \times A_2B_2$
9. $A_1B_1 \times A_3B_2$
10. $A_1B_1 \times A_1A_2B_2$
11. $A_1A_2B_1 \times A_1B_2$

The same logical approach as in the previous genetic system is applied to the phenotypes of the A factor when they are doubtful. For the B factor to be demonstrated to be heterozygous there must exist a B_2 child.

The various mating types together with their appropriate scores and amounts of information are set out in table 8.

The mating, $A_1A_2B_1 \times A_1B_1$, in table 8 will be used to illustrate setting up the generating function for the evaluation of scores, score correction factors and amounts of information. If in type 5 in table 8, there exist A_2 and B_2 children then the genotypes are determinate for both parents and the mating is:

$$A_1A_2B_1B_2 \times A_1A_3B_1B_2$$

The phenotypes of the mating are:

$$\begin{array}{llll} A_1B_1 & & & \\ A_1A_2B_1 & A_2B_1 & & \\ & & A_1B_2 & \\ & & A_1A_2B_2 & A_2B_2 \end{array}$$

and have for their probabilities:

$$\begin{array}{llll} \frac{2-\chi_1}{4} & & & \\ \frac{1-\chi_2+\chi_1\chi_2}{4} & \frac{\chi_1+\chi_2-\chi_1\chi_2}{4} & & \\ & & \frac{\chi_1}{4} & \\ & & \frac{(1-\chi_1)\,\chi_2}{4} & \frac{(1-\chi_1)\,(1-\chi_2)}{4} \end{array}$$

In scoring for χ_1, all six phenotypes will be used in the score but in scoring for χ_2, phenotypes, A_1B_1 and A_1B_2 contribute nothing to the detection of linkage and so will be rejected, leaving four phenotypes to be

Table 8

Table of scores, one factor ABO blood group, other factor dominant

Type	Mating by phenotypes	If there exist children	Mating is proven to be	χ	a	b	c	d	λ	$\overline{\lambda}$	I	Reject children	*Finney's* type
1	$A_1B_1 \times A_1B_1$	$A_3 \cdot B_2$	$A_1A_3B_1B_2 \times A_1A_3B_1B_2$	χ	A_1B_1	A_3B_1	A_1B_2	A_3B_2	$^1/_{81}u_{33}$	ε_7	ω_7		15
2	$A_1A_2B_1 \times A_1A_2B_1$	B_2	$A_1A_2B_1B_2 \times A_1A_2B_1B_2$	χ	A_2B_1	A_2B_2	A_1B_1	A_1B_2	$^1/_9u_{31}$		$4\ \omega_2$	(A_1A_2)	19
3	$A_1B_1 \times A_2B_1$	$[A_3(A_1 \cdot A_2)] \cdot B_2$	$A_1A_3B_1B_2 \times A_2A_3B_1B_2$	χ_1	A_2B_1	A_2B_2	$A_1A_2B_1$	$A_1A_2B_2$	$^1/_{18}u_{31}$	ε_6	ω_6		
					A_3B_1	A_3B_2	A_1B_1	A_1B_2					
				χ_2	A_1B_1	A_1B_2	$A_1A_2B_1$	$A_1A_2B_2$	$^1/_{18}u_{31}$	ε_6	ω_6		
					A_3B_1	A_3B_2	A_2B_1	A_2B_2					
		$(A_2{\sim}A_1{\sim}A_3) \cdot B_2$	$A_1A_3B_1B_2 \times A_2B_1B_2$	χ_1	$A_1A_2B_1$	A_2B_2	$A_1A_2B_1$	A_2B_2	$^1/_{18}u_{31}$	ε_6	ω_6		14
4	$A_1B_1 \times A_3B_1$	$A_3 \cdot B_2$	$A_1A_3B_1B_2 \times A_3B_1B_2$	χ_1	A_3B_1	A_3B_2	A_1B_1	A_1B_2	$^1/_{18}u_{31}$	ε_6	ω_6		14
5	$A_1A_2B_1 \times A_1B_1$	$A_2 \cdot B_2$	$A_1A_2B_1B_2 \times A_1A_3B_1B_2$	χ_1	$A_1A_2B_1$	$A_1A_2B_2$	A_1B_1	A_1B_2	$^1/_{18}u_{31}$	$^1/_2\varepsilon_7$	ω_{101}		
					A_2B_1	A_2B_2							
				χ_2	A_2B_1	A_2B_2	$A_1A_2B_1$	$A_1A_2B_2$	$^1/_{18}u_{31}$	ε_6	ω_6	(A_1)	
		$({\sim}A_2) \cdot B_2$	$A_1A_2B_1B_2 \times A_1B_1B_2$	χ_1	$A_1A_2B_1$	$A_1A_2B_2$	A_1B_1	A_1B_2	$^1/_{18}u_{31}$		ω_2		18
6	$A_1B_1 \times A_1B_2$	$A_3 \cdot B_2$	$A_1A_3B_1B_2 \times A_1A_3B_2$	χ_1	A_1B_2	A_3B_2	A_1B_1	A_3B_1	$^1/_{18}u_{31}$	ε_6	ω_6		14
7	$A_1A_2B_1 \times A_1A_2B_2$	B_2	$A_1A_2B_1B_2 \times A_1A_2B_2$	χ_1	A_1B_1	A_1B_2	A_2B_1	A_2B_2	$^1/_2u_{11}$		ω_1	(A_1A_2)	17
8	$A_1B_1 \times A_2B_2$	$[A_3(A_1 \cdot A_2)] \cdot B_2$	$A_1A_3B_1B_2 \times A_2A_3B_2$	χ_1	$A_1A_2B_1$	A_2B_1	$A_1A_2B_2$	A_2B_2	$^1/_2u_{11}$	ε_5	ω_5		
					A_1B_1	A_3B_1	A_1B_2	A_3B_2					
		$(A_2{\sim}A_1{\sim}A_3) \cdot B_2$	$A_1A_3B_1B_2 \times A_2B_2$	χ_1	$A_1A_2B_1$	A_2B_1	$A_1A_2B_2$	A_2B_2	$^1/_2u_{11}$	ε_5	ω_5		
9	$A_1B_1 \times A_3B_2$	$A_3 \cdot B_2$	$A_1A_3B_1B_2 \times A_3B_2$	χ_1	A_1B_1	A_3B_1	A_1B_2	A_3B_2	$^1/_2u_{11}$	ε_5	ω_5		13
10	$A_1B_1 \times A_1A_2B_2$	$A_2 \cdot B_2$	$A_1A_3B_1B_2 \times A_1A_2B_2$	χ_1	$A_1A_2B_1$	A_2B_1	$A_1A_2B_2$	A_2B_2	$^1/_2u_{11}$	ε_5	ω_5	(A_1)	13′
11	$A_1A_2B_1 \times A_1B_2$	$({\sim}A_2) \cdot B_2$	$A_1A_2B_1B_2 \times A_1B_2$	χ_1	A_1B_1	$A_1A_2B_1$	A_1B_2	$A_1A_2B_2$	$^1/_2u_{11}$		ω_1		16′

used in the score for this parent. The generating function, Φ_1, for the χ_1 score is

$$\Phi_1 = (1, 2. \ldots. 6)^s - (1, 2, 3)^s - (1, 2, 4, 5)^s + (1, 2)^s.$$

The frequency of admissible families is:

$$\overline{F}_1 = \frac{(4^s - 3^s)^2}{16^s}$$

Application of *Bailey*'s simplified method to the above generating function gives:

$$\lambda_1 = {}^1/_{18}\, u_{31}$$

$$\overline{\lambda}_1 = {}^1/_2 \frac{s\,(s-1)\,9^{s-2}}{(4^s - 3^s)^2} = {}^1/_2\, \varepsilon_7$$

$$I_1 = {}^1/_{18} \frac{s\,(s-1)}{(4^s - 3^s)^2} \left[16^s - 12^s - 3^{s-2}\,4^s + 9^{s-s} J_1\right] - {}^1/_4\, \varepsilon_7^2$$

$$I_1 = \omega_{101}$$

$$\text{where } J_1 = 9^2 + 2.9\,(s-2) + \tfrac{1}{2}s\,(s-1)$$

For the χ_2 score, A_1 children are rejected as they contribute no information to linkage, χ_2. This leaves phenotypes:

$$A_1A_2B_1,\ A_2B_1,\ A_1A_2B_2,\ A_2B_2,$$

with probabilities:

$$\frac{1 - \chi_2 + \chi_1\chi_2}{2}, \quad \frac{\chi_1 + \chi_2 - \chi_1\chi_2}{2}, \quad \frac{(1-\chi_1)\,\chi_2}{2}, \quad \frac{(1-\chi_1)\,(1-\chi_2)}{2}$$

The generating function, Φ_2, for the χ_2 score is:

$$\Phi_2 = (1, 2, 3, 4)^s - (1, 2)^s - (1, 3)^s + (1)^s.$$

Application of *Bailey*'s simplified approach gives:

$$\lambda_2 = {}^1/_{18}u_{31}$$
$$\overline{\lambda}_2 = \varepsilon_6$$
$$I_2 = \omega_6$$

Summary

Scoring procedures using u-statistics are developed for more complex types of matings when one or both of the loci of two factors have a series of at most four allelomorphic genes.

Expressions for the scores, score correction factors and amounts of information are developed fully for several genetic systems, so that a test for linkage may be made and if the null hypothesis is contradicted, an estimate of linkage may be found. Two portions of the score, corresponding to the two recombination fractions, are derived and given in the tables. Three procedures involving the recombination fractions of each parent are discussed and one procedure is adopted in the paper.

Scoring procedures for the genetic system with neither factor showing dominance are developed in detail. The scoring statistics for six mating types (of which three are new) are tabulated.

Scoring procedures for one factor, the ABO blood group system, and the other factor of two genes:

(1) showing non-dominance,
(2) showing dominance,

are developed and tabulated.

Zusammenfassung

Die u-Statistik zum Nachweis autosomaler Genkoppelung beim Menschen *(Fisher/Finney)* wird für kompliziertere Paarungstypen weiter ausgebaut. Es werden diejenigen Fälle einbezogen, in denen einer oder beide loci eine Serie von höchstens vier allelen Genen besitzen.

Ausdrücke für die u-scores, Korrekturfaktoren und Ausdrücke für die Information werden für verschiedene genetische Systeme ausführlich entwickelt, so daß auf Koppelung geprüft und – falls die 0-Hypothese nicht zutrifft – eine Schätzung der Rekombinationswahrscheinlichkeit gefunden werden kann.

Zwei den Rekombinationswerten entsprechende Teile des score werden abgeleitet und in den Tabellen zusammengestellt. Drei Methoden, die die Rekombinationswerte jedes Elternteiles für sich einschließen, werden diskutiert. Eine von ihnen ist in dieser Arbeit angewendet worden.

Eingehend entwickelt werden scoring-Methoden für das genetische System, bei dem kein Faktor Dominanz zeigt. Die scoring-Verfahren für 6 Paarungstypen (darunter 3 neue) sind in Tabellen zusammengestellt.

Scoring-Methoden für einen Faktor, das ABO-System, und für zwei verschiedene Möglichkeiten bei dem anderen Faktor – keine Dominanz, Dominanz – werden entwickelt und tabellarisiert.

Résumé

En se basant sur des u-statistiques l'auteur développe des méthodes d'estimation pour des accouplements complexes dans lesquels les 2 loci de 2 facteurs peuvent être représentés par quatre gènes allèles au maximum.

Des formules pour les estimations ainsi que les facteurs de correction et le degré d'information sont données pour différents systèmes de génétique, ce qui permet de faire un test de linkage et estimer sa valeur au cas où l'hypothèse zéro est infirmée. L'auteur donne des tables dans lesquelles les 2 parties des estimations correspondant aux 2 taux de recombinaison sont indiquées. Pour le taux de recombinaison de chaque parent 3 méthodes sont discutées dont une est retenue dans ce travail.

Des procédés d'estimation pour des systèmes de génétique sans facteur dominant sont développés en détail. Les valeurs d'estimation pour 6 types d'accouplement (dont 3 nouveaux) sont réunies dans des tables.

En outre la méthode d'estimation pour un facteur représenté par le système ABO et un 2e facteur à 2 gènes sans et avec dominance est également calculée.

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LIBRI

Proceedings of the X International Congress of Genetics, August 20-27, 1958. Vol. I and II. University of Toronto Press, Toronto, Ontario, Canada. 1958/59. £ 7.7.0.

The complete Proceedings of the 1958 Congress of Genetics in Montreal are now available. Vol. II, containing abstracts of the proffered papers, was sent out last year when the Congress opened, and vol. I has recently been published giving the main lectures as well as other reports. It has thus been achieved to complete the publications of the Congress within one year after it was held. Vol. II contains only very short introductions to or summaries of the major part of the papers, which were read at the Congress, and no references as to the place of publication of the detailed reports are given. The lack of an index of subjects makes it difficult to find works of special interest to the reader.

Vol. I gives all the details of the organisation of the Congress, the full records of the inaugural session and of special convocations, the minutes of the business meeting, and the highly interesting "story" of the Congress, which clearly demonstrates the tremendous work imposed on those, who devoted years of their life to the organisation and administration of the Congress. Five years of hard work lay behind the success. Most of the lectures given at the seven symposia are found here. These symposia dealt with the structure of genetic material, cytogenetics and plant breeding, genetics in animal breeding, mutation and mutagenesis, physiological genetics, genetics in evolution and advances in human genetics. Furthermore, three special lectures are included: on a new category of chromosomes, by *A. Müntzing*, on genetics and the destiny of man, by *Dobzhansky*, and finally a paper on genetics, the gene, and the hierarchy of biological sciences by the president of the Congress, *Sewall Wright*. Two panel discussions concerning the teaching of genetics and Drosophila terminology are also reported. Apart from the special symposium on human genetics, many of the other papers are of great value even to those, who are only dealing with human genetics, because they introduce many new ideas and fruitful thoughts and throw new and better lights on many of the basic principles in genetics, which are essential also to human geneticists. The symposium on human genetics was opened with a lecture by *Böök* on schizophrenic psychoses. A very interesting survey of the biochemical studies in this group of diseases is given, and *Böök* suggests that the results indicate that at least some of these psychoses may be caused by a genetically determined defect in those enzyme systems which maintain homeostasis by the breakdown of substances produced during stress. New studies of the biochemical effects of major gene differences are certainly needed.

Lamy and Frézal report extensive investigations on the etiology of twinning which confirmed earlier statements as to the significant rôle of heredity in the production of dizygous twins. *Harris* gives a few examples of recently disclosed biochemical aberrations, and discusses the mechanisms which may be responsible for abnormal amounts of amino-acids in the urine. This can be caused not only by a block in intermediary metabolism but also by some renal defect, and it is suggested that inherited peculiarities in the transport of substances elsewhere in the body might easily mimic the kind of changes observed in blocks in intermediary metabolism. But mutant alleles may cause not only defects but also the formation of new proteins with qualitatively different enzymatic properties. Finally the recent advances in our knowledge of protein synthesis are treated. *Neel* gives an excellent survey of the aspects of the genetic control of the structure of the haemo-

globin molecule. This vast field, which practically did not exist ten years ago, has increased our knowledge on many basic genetic points and promises to give much more information on biochemical and population genetics. The symposium was closed by *Fraser Roberts*, who reviewed the present situation within another newly developed field, the associations between blood group and disease. New studies suggesting new significant associations were mentioned, and again they were with diseases of the gastro-intestinal tract. More investigations are certainly still needed and both positive and negative findings ought to be reported. This volume is fascinating and stimulating reading and is recommended to all who want a concentrated survey of our present knowledge within the major fields of genetics. *Mogens Hauge*, Copenhagen

David Yi-Yung Hsia: **Inborn Errors of Metabolism.** The Year Book Publ., Chicago, Ill. 1959. 358 p., 127 ill. $ 9.50.

The study of the diseases grouped under the heading "inborn errors of metabolism" demands not only clinical knowledge but also rather intimate knowledge of biochemistry and genetics and this, together with the comparative rarity of the individual syndromes, makes it difficult for the clinician to keep his knowledge concerning these diseases up to date. This handy little book by *Hsia* fills a great need in this respect. About 70 known defective metabolic states are presented clinically, genetically and pathologically in a brief but extremely clear manner. The text concerning each of the diseases is accompanied by particularly beautiful and clear plates to demonstrate the mode of inheritance as well as the biochemical defect involved and the resulting development of symptoms.

The abundant material is divided in a logical manner according to the biochemical character of the defect. A defect in the structure of the molecule is found in the various forms of abnormal haemoglobins, thalassaemia, *Pelger's* nuclear anomaly and a few other conditions. The complete absence of synthesis of special proteins is involved in agammaglobinaemia, ceruloplasmin deficiency (*Wilson*'s disease), congenital afibrogenaemia and the various forms of haemophilia (classical haemophilia, *Christmas* disease etc.). The most extensive section is devoted to the various known forms of enzyme defects in the metabolism of amino acids (phenylketonuria, alkaptonuria etc.), carbohydrate metabolism (fructosuria, galactosuria, hereditary spherocytosis, *vanGierke*'s disease etc.), pigment metabolism (porphyria, methaemoglobinaemia, familial non-haemolytic jaundice etc.) and endocrine metabolism (various forms of cretinism and suprarenal hyperplasia). A special section is devoted to disturbances in the renal transport apparatus (aminoaciduria, renal diabetes insipidus, renal glycosuria and *Fanconi*'s syndrome) and, finally, the last chapter deals with the numerous metabolic defects concerning which the pathogenesis is as yet incompletely elucidated (among these are the hyperlipaemiae, *Niemann-Pick*'s disease, various forms of muscular dystrophies together with diabetes mellitus and gout). It is of great practical significance that a very meticulous account is given in an appendix of the biochemical method in the diagnosis in the various deficiency states.

There can be no doubt that this little book will become invaluable for paediatritians, physicians, laboratory research workers and geneticists. The references to the literature are abundant and well classified although with a not inconsiderable Anglo-Saxon bias. The absence of any reference to *Becker*'s pioneer differentiation of the progressive muscular dystrophies is a regrettable omission and *Gamstorp*'s and *Sagild*'s episodic adynamia is not even mentioned. *Bent Harvald*, Copenhagen

M. Lamy, P. Royer et J. Frézal: **Maladies héréditaires du métabolisme chez l'enfant.** Masson et Cie, Paris 1959. 260 pages. 72 fig. Francs français 3600.

The authors of this book, who are closely connected with paediatrics as well as with human genetics, have intended to illustrate the importance and action of genes in paediatric diseases by means of a short survey of a number of metabolic deviations which may cause major diseases recognizable early in childhood. In addition to their own studies within this field they review most of our present knowledge concerning diseases due to disturbances in amino acid, lipid and carbohydrate metabolism, in the renal transport mechanism as well as a few other similar states of obscure etiology, i.e. diabetes mellitus, spontaneous hypoglycaemia, pituitary diabetes insipidus, cystic fibrosis of the pancreas and some adrenal disorders. Besides short clinical descriptions the features of anatomy, biochemistry, genetics, pathogenesis and therapy are summarized. It is clearly demonstrated that genetic knowledge is indispensable to all those who are attacking nosological, pathogenetic and therapeutical problems and in preventive medicine. An extensive bibliography accompanies the chapters and a short survey of the basic principles of genetics is given as an introduction, which should enable all physicians to use this book. The regrettable lack of an index of subjects will, however, reduce its value in daily work. The great current interest in these problems is reflected by the fact that one or two other books, covering much the same aspects, have appeared in the Anglo-Saxon world at the same time. *Lis Elmholt*, Copenhagen.

R. Huron et J. Ruffié: **Les méthodes en génétique générale et en génétique humaine.** Masson et Cie, Paris 1959. 556 pages. 79 fig. Francs français 8200.

The growing interest in human genetics and the need for more intensive and extensive studies within this field have made the lack of a comprehensive and up-to-date methodological manual increasingly conspicuous. The title of the present book suggests that it may have been the intention of the authors to fill this gap. It seems that nothing comparable to this volume has existed in France previously, but it is difficult to define the proper place and value of this book to English-reading people. They will probably find that the first part (130 pages) on general and formal genetics does not reach the level of the numerous short, but excellent introductions to genetics and human genetics which have appeared in England and America during the last 5–10 years. The main part of the book (400 pages) describes most of the current statistical methods used by geneticists and in most cases examples of their application are given. It does not contain very much more than is found in the well known books in English on these subjects. A register rerum is included but the bibliography is extremely limited. The amount of errata is disturbingly high. *Mogens Hauge*, Copenhagen

VARIA

Teratology Society. For several years scientists interested in basic problems of congenital malformations have held informal conferences in which questions of common interest were discussed. Anatomists, biochemists, embryologists, geneticists, obstetricians, pathologists, pediatricians, plastic surgeons and others attended these conferences which were in part supported by the Association for the Aid of Crippled Children, New York, N.Y., and the Human Embryology and Development Study Section of the National Institutes of Health. With the increased interest in recent years in this area, it was felt

that there was a need for a Society to hold regular meetings in which investigations concerned with etiology and morphogenesis of congenital malformations could be presented and discussed. Following the fourth teratology conference, which was held at the Memorial Sloan-Kettering Cancer Center in New York City and attended by 76 scientists from Canada, England, France, Germany and the U.S.A., "The Teratology Society" was formed for the purposes outlined above. The following officers were elected: President: *Josef Warkany*, M.D., Cincinnati, O.; President-Elect: *James G. Wilson*, Ph.D., Gainesville, Fla.; Secretary-Treasurer: *Marjorie M. Nelson*, Ph.D., San Francisco, Calif.; Recorder: *Sidney Q. Cohlan*, M.D., New York, N.Y.; Council: *F. Clarke Fraser*, Ph.D., M.D., Montreal, Canada, *David L. Gunberg*, Ph.D., Portland, Ore., and *M. Lois Murphy*, M.D., New York, N.Y. The National Foundation assisted in the formation of the Society with advice and financial aid. Inquiries about The Teratology Society should be directed to Dr. *Marjorie M. Nelson*, Department of Anatomy, School of Medicine, University of California, San Francisco 22, Calif.

1er congrès international d'histochimie et de cytochimie. Paris 28 août – 3 septembre 1960. Président: Professeur *J. Verne*. Secrétaire Général: D^r^ *R. Wegmann*, 45, rue des Saints-Pères, Paris (6^e^).

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D'autres sujets de rapports seront précisés dans un programme ultérieur.

Toute la correspondance relative au Congrès peut être adressée à: D^r^ R. Wegmann, Institut d'Histochimie Médicale, 45, rue des Saints-Pères, *Paris* (6^e^), France. Le programme détaillé sera envoyé sur demande. Inscription: Membres actifs 25 $; membres associés 20 $.

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